CURRICULUM VITAE

INFORMAZIONI PERSONALI

Nome	**PIETRO CACIALLI**
Indirizzo	RUE JEAN-VIOLETTE 3, 1205 GINEVRA, SVIZZERA.
Telefono	-
Fax	-
E-mail	**pietro.cacialli@unige.ch**
Nazionalità	Italiano
Data di nascita	28-12-1986

ISTRUZIONE E TITOLI DI STUDIO

• 2016 Consegue il **Dottorato di ricerca** in: "Organismi modello nella ricerca biomedica e veterinaria", in aggiunta il Label "**Doctor Europaeus"**, presso l'Università degli Studi di Napoli Federico II. Titolo della tesi: "Brain derived neurotrophic factor (BDNF) expression in postnatal and adult zebrafish brain and related changes following mechanical injury". Relatore: Prof. Carla Lucini

• 2013 **Corso di perfezionamento post-laurea** in: "Biologia e tecnologia della riproduzione assistita", conseguito presso l'Università degli Studi di Napoli Federico II. Direttore del corso: Prof. Riccardo Talevi.

• 2012 Consegue la **Laurea Magistrale (LM-06)** in: "Biologia della riproduzione e del differenziamento cellulare", presso l'Università degli Studi di Napoli Federico II. Titolo della tesi: "La microscopia olografica digitale nell'analisi tridimensionale dello spermatozoo umano". Relatore: Prof. Riccardo Talevi; Correlatore: Prof. Brian Dale; Supervisore: Dr. Gianfranco Coppola

• 2009 Consegue la **Laurea triennale (L-12)** in: "Biologia generale ed applicata" conseguita presso l'Università degli Studi di Napoli Federico II. Titolo della tesi di laurea triennale: "Il monitoraggio igienistico della carne". Relatore: Prof. Francesco Aliberti

ESPERIENZE LAVORATIVE DI RICERCA

2021 – 2022 **Vincitore del concorso come Maitre-Assistant**, presso la Facoltà di Medicina dell'Università di Ginevra, (Svizzera).

2016 – 2021 **Ricercatore post-doc,** presso il laboratorio del Prof. Julien Bertrand nel Dipartimento di Patologia ed Immunologia dell'Università di Ginevra, in Svizzera. Progetto di ricerca: "Study of the molecular and cellular pathways involved in Hematopoietic Stem Cells (HSCs) expansion in the fetal niche".

• 2013 - 2016	**Dottorando di ricerca** in "Organismi modello nella ricerca biomedica e veterinaria", presso il laboratorio di anatomia animale ed embriologia diretto dalla Prof. Luciana Castaldo nel Dipartimento di Medicina Veterinaria dell'Università degli Studi di Napoli Federico II. 1) Progetto di ricerca: "The role of BDNF and its receptor TrkB during zebrafish oocyte development" 2) Progetto di ricerca: "Study of BDNF during neural repair after traumatic brain injury in adult zebrafish"
• 2014 - 2015	**"Premio di mobilità per la ricerca",** assegnata dalla commissione dei Dottorati di ricerca (Vie-Agro-Santè) dell'Università di Rennes in Francia**,** per un periodo di ricerca svolto presso l'Institut de Recherche en Santé, Environnement et Travail (IRSET), nel laboratorio diretto dal Professore Emerito Olivier Kah**.** Progetto di ricerca: "The role of Brain-Derived Neurotrophic Factor (BDNF) and Estradiol (E2) during regeneration of the adult zebrafish brain."
• 2010 - 2012	**Biologo in training**, presso il Centro di Fecondazione Assistita (CFA) della Clinica Villa del Sole di Napoli diretto dal Professore Brian Dale. Progetto di ricerca: "Digital Holography Microscopy in 3D analysis of human sperm".
• 2007 - 2008	**Collaborazione part-time (borsa di studio Federico II**), svolta presso il Dipartimento di Scienze Biologiche dell'Università degli Studi di Napoli Federico II, diretto dal Professore Luciano Gaudio.

BORSE DI STUDIO E PREMI DI RICERCA

• 2018-2021	**Vincitore di un contratto di Ricercatore post-doc presso l'Università di Ginevra in Svizzera**, (Fondi per la ricerca del cantone di Ginevra)
• 2019	**Vincitore del Premio miglior presentazione orale alla conferenza internazionale "Zebrafish Disease Models 12"**, dal 15-18 Luglio, tenutasi presso la Harvard Medical School, Boston, USA.
• 2016 - 2018	**Vincitore di un contratto di Ricercatore post-doc presso l'Università di Ginevra in Svizzera,** (Prof. Julien Bertrand).
• 2014 – 2015	**Vincitore di un "Premio di mobilità per la ricerca", assegnato dalla commissione dei Dottorati di ricerca (VAS) dell'Università di Rennes in Francia,** per un periodo di ricerca svolto presso l'Institut de Recherche en Santé, Environnement et Travail (IRSET).
• 2013 -2016	**Vincitore del concorso di Dottorato di Ricerca con Borsa di studio (MIUR), presso l'Università degli Studi di Napoli Federico II**. 28°ciclo in**:** "Organismi modello nella ricerca biomedica e veterinaria",
• 2012 - 2013	**Vincitore della Borsa di Studio "Homo Sapiens" dell'INPS,** per il conseguimento del corso di perfezionamento post-laurea in "Biologia e tecnologia della riproduzione assistita" dell'Università degli Studi di Napoli Federico II.

• 2007 - 2008 **Vincitore del concorso per contratti di collaborazioni part-time,** dell'Università degli Studi di Napoli Federico II.

FINANZIAMENTI COME PRINCIPAL INVESTIGATOR

2021 **Gestione e coordinamento di un finanziamento ottenuto come Principal investigator (Under 40), Dr. Pietro Cacialli**, ***Ernest Boninchi Foundation,* 30'000 CHF.** Università di Ginevra, Svizzera**.** Titolo del progetto: *"Autophagy: a new therapeutic target to restore synaptic dysfunction in Lysosomal Storage Diseases"*.

2020 **Gestione e coordinamento di un finanziamento ottenuto come Principal investigator (Under 40), Dr. Pietro Cacialli**, ***Gertrude Von Meissner Foundation*, 50'000 CHF.** Università di Ginevra, Svizzera. Titolo del progetto: "*The neuropathology of lysosomal storage diseases: insight from a zebrafish model"*.

ATTIVITA' DI INSEGNAMENTO

2021-2022 **16 ore di attività didattica per il modulo "Interazione Cellulare" (anno accademico 2021-2022)**, Scuola di dottorato in scienze della vita presso l'Università di Ginevra (Svizzera).

2020-2022 **52 ore di attività didattica per i seguenti moduli:**
Anatomia comparata (12 ore nell'anno accademico 2020-2021)
Anatomia comparata (12 ore nell'anno accademico 2021-2022)
Biologia dello sviluppo (14 ore nell'anno accademico 2020-2021),
Biologia dello sviluppo (14 ore nell'anno accademico 2021-2022)
per gli studenti del corso di laurea triennale in Scienze Biomediche presso la Facoltà di Medicina dell'Università di Ginevra (Svizzera).

2017-2022 **Training e supervisione di 2 tesi di studenti del corso di laurea (Master), candidati:** Serkan Dogan (Title: mcm10 regulates the emergences of HSCs from the dorsal aorta of zebrafish embryo, 2021); Julien Angiolillo (Title: cndp2 is involved in expansion of HSCs in the CHT of zebrafish embryo, 2020) **e 4 tesi di dottorato (Scuola di dottorato in Scienze della vita), per i seguenti candidati:** Tanya Linnerz (dottorata nel 2018); Joey J. Ghersi (dottorato nel 2018); Etienne Gomez (in corso); Tim Petzold (in corso) presso il laboratorio diretto dal Professore Julien Bertrand nell'Università di Ginevra (Svizzera).

2013 - 2016 **60 ore di didattica integrativa per i seguenti moduli: Anatomia degli animali, Citologia ed Istologia, Embriologia e Morfogenesi.** Per gli studenti del corso di laurea a ciclo unico in Medicina Veterinaria e laurea triennale in Tecnologie delle produzioni animali dell'Università degli Studi di Napoli Federico II.

ATTIVITA' DI REVISORE ED EDITORE PER RIVISTE

• 2019 – 2022 — **Attività di revisore** delle riviste scientifiche "Neural Regeneration Research", "Plos One", "Blood Advances", "International Journal of molecular Sciences", "Genes", Neuroscience Letter", "Brain Sciences", "Cells", "Biology", "Biomedicines", etc.

2021 — **Editore per la rivista JoVE,** collection "Teleost Species as a Tool for Regenerative Medicine".

ULTERIORI RUOLI ORGANIZZATIVI ED ISTITUZIONALI

2021-2022 — **Membro del Dipartimento di Patologia ed Immunologia dell'Università di Ginevra, responsabile dell'organizzazione di seminari e progress report. (Lettera del Direttore di Dipartimento).**

2022 — **Membro responsabile dell'organizzazione degli esami federali per medici, su mandato firmato dal Vice-Preside della Facoltà di Medicina dell'Università di Ginevra, Prof. Mathieu Nandez** (Organisation de l'examen fédéral de médecine humaine (EFMH) 2022 et sur mandat du Vice-doyen de l'enseignement, le Professeur Mathieu Nendaz).

ASSOCIAZIONI SCIENTIFICHE

• 2019-2021 — **Membro EuFishBiomed.**

• 2018-2019 — **Membro della Zebrafish Disease Model Association.**

LINGUE

ITALIANO — **Madre lingua**

INGLESE — **LIVELLO C2 (certificato BULATS)**

FRANCESE — **LIVELLO B2 (certificato IFAGE conseguito a Ginevra)**

COMPETENZE TECNICHE

BIOLOGIA MOLECOLARE	□ Estrazione di RNA e DNA □ PCR, RT-PCR, Real-Time PCR □ Trasformazione batterica □ Mini-prep, Midi-prep, Maxi-prep □ Clonaggio e linearizzazioni plasmidi □ Sequenziamento □ Test (Tunel) □ Ibridazione in situ (ISH)
GENETICA	□ Generazione di animali transgenici (gain of function) □ Generazione di mutanti utilizzando CRISPR/cas9 □ Morpholino strategy (gene knock-down)
BIOINFORMATICA	□ BLAST, ENSEMBL □ APE, NGS, RNA-seq
ESPERIENZA CON ANIMALI DA LABORATORIO	□ Manutenzione di una facility di zebrafish □ Micro-iniezione in embrioni di zebrafish □ Iniezione Intra-cerebroventricolare nel cervello di zebrafish □ Test in vivo per analizzare i livelli di stress metabolico ed ossidativo
TECNICHE IMMUNOISTOCHIMICHE	□ Inclusione in paraffina □ Taglio al microtomo e criostato □ Colorazioni istologiche □ ABC (Avidin-Biotin); DAB □ Immunofluorescenza
CITOMETRIA	□ FACS cell sorting
MICROSCOPIA	□ Microscopia Confocale □ Microscopia a fluorescenza □ Microscopia a contrasto differenziale (DIC) □ Microscopia olografica digitale (DHM-3D)
BIOLOGIA DELLA RIPRODUZIONE	□ IVM □ IVF □ Analisi del liquido seminale ed ovociti □ Fivet, ICSI

<u>Relatore (speaker)</u> alle seguenti conferenze nazionali ed internazionali

1) **<u>Cacialli P.,</u>** Bertrand J.Y. A connexin/ifi30 pathway bridges HSCs with their niche to dampen oxidative stress. (Oral presentation) Second PANACHE Meeting, 22 Novembre 2021, (virtual-zoom).

2) **<u>Cacialli P.</u>**, Bertrand J.Y. "Myeloid and vascular cells cooperate to expand HSCs in the embryonic hematopoietic niche". (Oral presentation) 13th Swiss Zebrafish Society Annual Meeting, 8-9 April 2021 (virtual-zoom).

3) **<u>Cacialli P.</u>**, Bertrand J.Y. "The cooperation between myeloid and vascular cells favors HSC expansion in the embryonic hematopoietic niche". (Poster) 11th European Zebrafish Meeting, 26-28 October 2020 (virtual-zoom).

4) **<u>Cacialli P.</u>**, Bertrand J.Y. The endothelial niche detoxifies HSCs from ROS in the caudal hematopoietic tissue. (Oral Presentation) Zebrafish disease model conference ZDM12, 15-18 Luglio 2019, Harvard Medical School, Boston, USA.

5) **<u>Cacialli P</u>**., Gatta C., D'Angelo L., Leggieri A., Palladino A., de Girolamo P., Pellegrini E., Lucini C. Nerve growth factor is expressed and stored in brain neurons of adult zebrafish. (Poster) 8th meeting of Neapolitan Brain Group (NBG), 13 Dicembre 2018, Universita' degli Studi di Napoli Federico II.

6) **Cacialli P**., <u>Bertrand J.Y</u>. The vascular niche protects embryonic HSCs from ROS through IFI30. (Poster) EMBL Conference Heidelberg, Germania 7 - 9 Giugno 2018.

7) **<u>Cacialli P</u>**., Bertrand J.Y. Zebrafish gamma-interferon-inducible lysosomal thiol reductase (ifi30), a new target of the transcription factor tfec, expands hematopoietic stem cells. (Poster) 13th Swiss Stem Cell Network, 5 Settembre 2017, Università di Losanna (CHUV), Svizzera.

8) **<u>Cacialli P</u>**., D'Angelo L., de Girolamo P., Castaldo L., Kah O., Coumailleau P., Pellegrini E., Lucini C. Brain derived neurotrophic factor (BDNF) expression is associated with neural repair of injured adult zebrafish telencephalon. (Poster) 10th annual Swiss Zebrafish Meeting, 27 Gennaio 2017, Berna, Svizzera.

9) **<u>Cacialli P</u>**., Pellegrini E., Kah O., Castaldo L. Brain derived neurotrophic factor (BDNF) and its receptor TrkB during zebrafish oocyte development. (Oral Communication) 10° Congresso dell'Associazione dei Morfologi Veterinari, 20-21 Maggio 2015, Roma. Annals of Anatomy September 2016 DOI: 10.1016/j.aanat.2016.04.006

10) **<u>Cacialli P</u>**., D'angelo L., De Girolamo P., Lucini C., Pellegrini E., Kah O., Castaldo L. Brain derived neurotrophic factor in zebrafish ovary. (Poster) 1th Reproscience Congress, 13-15 Aprile 2015, Campus Bealieau, Università di Rennes, Francia.

LISTA DI PUBBLICAZIONI

1) Russo B., Borowczyk J., **Cacialli P.**, Moguelet P., Truchetet M.E., Modarressi A., Brembilla N.C., Bertrand J., Boehncke W.H., Chizzolini C. "IL-25 participates in keratinocyte-driven dermal matrix turnover and is reduced in Systemic Sclerosis epidermis" (**Rheumatology**, Oxford. 2022 Feb 16:keac044. doi: 10.1093/rheumatology/keac044. Epub ahead of print. PMID: 35171244).

2) **Cacialli P.,** Mahony C.B., Petzold T., Bordignon P., Rougemont AL. and Bertrand J.Y. "A *connexin/ifi30* pathway bridges HSCs with their niche to dampen oxidative stress". (**Nature Communications** 2021**,** Jul 23; 12 (1): 4484 doi: 10.1038/s41467-021-24831-0).

3) Ricci S., **Cacialli P.** "Stem Cell Research Tools in Human Metabolic Disorders: an Overview". (**Cells** 2021, Oct 7;10(10):2681. doi: 10.3390/cells10102681).

4) Mahony C.B., **Cacialli P.**, Pasche C., Montero R., Savvides S., Bertrand J.Y. "Hapln1b organizes the ECM to modulate kit signaling and control developmental hematopoiesis in zebrafish". (**Blood Advances** 2021, Sep 20; doi: 10.1182/bloodadvances.2020001524).

5) **Cacialli P**. "Neurotrophins Time Point Intervention after Traumatic Brain Injury: From Zebrafish to Human". (**International Journal of Molecular Sciences**. 2021 Feb 4;22(4):1585. doi: 10.3390/ijms22041585).

6) **Cacialli P**., Gatta C., D'Angelo L., Leggieri A., Palladino A., de Girolamo P., Pellegrini E., Lucini C. Nerve growth factor is expressed and stored in brain neurons of adult zebrafish. (**Journal of Anatomy** 2019 Jul;235(1):167-179. doi:10.1111/joa.12986).

7) **Cacialli P**., Lucini C. "Adult neurogenesis and regeneration in zebrafish brain: are the neurotrophins involved in?". (**Neural Regeneration Research** 2019 Dec;14(12):2067-2068. doi:10.4103/1673-5374.262574).

8) **Cacialli P**., D'angelo L., Kah O., Coumailleau P., Gueguen M.M., Pellegrini E., Lucini C. Neuronal expression of Brain Derived Neurotrophic Factor in the injured telencephalon of adult zebrafish. (**Journal of Comparative Neurology,** 2018 Mar 1;526(4):569-582. doi: 10.1002/cne.24352. Epub 2017 Nov 26.).

9) **Cacialli P**., Palladino A., Lucini C. The role of BDNF during the Regenerative Response after Traumatic Brain Injury in adult zebrafish. (**Neural Regeneration Research**, 2018 Jun;13(6):941-944. doi: 10.4103/1673-5374.233430).

10) **Cacialli P**., D'angelo L., de Girolamo P., Avallone L., Lucini C., Pellegrini E., Castaldo L. Morpho-functional features of the gonads of Danio rerio: the role of brain derived neurotrophic factor. (**The Anatomical Record**, 2018 Jan;301(1):140-147. doi: 10.1002/ar.23702. Epub 2017 Oct 27).

11) Lucini C, D'Angelo L, **Cacialli P**, Palladino A, de Girolamo P. BDNF, Brain, and Regeneration: Insights from Zebrafish. (**International Journal of Molecular Sciences**. 2018 Oct 13;19(10). doi:10.3390/ijms19103155).

12) **Cacialli P**., Gueguen M.M., Coumailleau P., Kah O., D'Angelo L., Lucini C., Pellegrini E. BDNF expression in larval and adult zebrafish brain: distribution and cell identification. (**Plos One**, 2016 Jun 23;11(6):e0158057. doi: 10.1371/journal.pone.0158057. eCollection 2016).

Firma Data 05/04/2022

UNIVERSITÀ DEGLI STUDI DI NAPOLI FEDERICO II
Dipartimento di Medicina Veterinaria e Produzioni Animali

Via F. Delpino 1 80137 Napoli – Tel. 0812536099 - Fax 0812536097

Attività didattica-integrativa

del Dott. Pietro Cacialli

Il Dott. Pietro Cacialli negli anni accademici (dal 2013 al 2016) ha effettuato 60 ore totali di didattica integrativa per i seguenti corsi di studio:

1) Anatomia degli animali domestici (corso di laurea a ciclo unico in Medicina veterinaria, e corso di laurea triennale in tecnologie delle produzioni animali), 20 ore.

2) Citologia ed Istologia (corso di laurea a ciclo unico in Medicina veterinaria, e corso di laurea triennale in tecnologie delle produzioni animali), 20 ore.

3) Embriologia e Morfogenesi (corso di laurea a ciclo unico in Medicina veterinaria, e corso di laurea triennale in tecnologie delle produzioni animali), 20 ore.

Napoli, 30/11/2015

Prof. Paolo de Girolamo
Università degli Studi di Napoli Federico II
Tel: +390812536099 Fax: +390812536097

UNIVERSITÀ DEGLI STUDI DI NAPOLI FEDERICO II – Dipartimento di Medicina Veterinaria e Produzioni Animali

UNIVERSITÉ DE GENÈVE

FACULTÉ DE MÉDECINE
CMU - rue Michel-Servet 1 |
Pathologie et Immunologie
CH-1211 Genève 4

Geneva, February 28th, 2022

TO WHOM IT MAY CONCERN

We, the undersigned, certify that :

Dr. Pietro CACIALLI, born 28/12/1986, Italian nationality

was first hired as a full-time **Post-doctoral employee** by the University of Geneva (Pathology and Immunology Dept.) as per December 1st, 2016 until September 30th, 2021. Dr. Cacialli currently holds the position of **Maitre-Assistant** within the same Department since October 1, 2021, at a rate of activity of 100% (research and teaching). During this period he taught as tutor for the Faculty of Medicine, for students of PhD School of Life Sciences (Cell Interaction module 16 hours), and for students of the Bachelor's in Biomedical Sciences, for the following modules:

- Developmental biology 28 hours in total (14 hours on 2020; 14 hours on 2021)
- Comparative anatomy 24 hours in total (12 hours on 2020; 12 hours on 2021)

Dépt Pathologie et Immunologie
C.M.U.
1, rue Michel Servet
CH -1211 Genève 4

I. JONKER

Ilse JONKER
Human Resources & Administration
Pathology and Immunology Dept.
Medecine Faculty
University of Geneva

UNIVERSITÉ DE GENÈVE

Contrat individuel de travail de droit privé
Personnel enseignant

Employeur

Université de Genève

Faculté de médecine

Département de pathologie et immunologie

Employé

Monsieur
Pietro CACIALLI

Rue ~~Prévost-Martin 38~~ des Voisins 8
1205 Genève
Suisse

Genève, le 01.12.2016

Ce contrat est conclu aux conditions suivantes :

1. Fonction : post-doctorant

2. Taux d'activité : 100 %

3. Le présent contrat est conclu pour la période du 1er décembre 2016 au 30 novembre 2017

   (le contrat prend fin, même sans résiliation préalable, à la date prévue ci-dessus, sauf reconduction écrite entre les parties, par avenant au présent contrat)

4. Traitement initial Classe : 14 Annuité : 0
   correspondant à un salaire brut annuel de CHF 81'347.00 , soit mensuel de CHF 6'257.50 | X 13

5. Période d'essai et/ou autres conditions :
   Les trois premiers mois constituent une période d'essai pendant laquelle il peut être mis un terme au contrat de part et d'autre, moyennant un préavis d'un mois pour la fin d'un mois.

6. Le statut des membres du corps enseignant rémunérés par des fonds provenant de l'extérieur est régi par le titre V du règlement sur le personnel. Un extrait des dispositions principales applicables du règlement sur le personnel de l'Université ,complété par des dispositions spécifiques, est à disposition au lien suivant :
   http://www.unige.ch/collaborateurs/nouveaux/lois.html

7. Il appartient à l'employé de nous informer immédiatement sur toute modification qui surviendrait dans les renseignements fournis (adresse, situation de famille, etc.)

Les parties déclarent :
- se conformer au présent contrat de travail
- avoir pris connaissance des dispositions légales citées qui font partie intégrante du présent engagement et en avoir accepté la teneur

Date et signature de l'employeur :

5.12.16

Date et signature de l'employé :

07/12/2016

Distribution : 1 exemplaire à l'employeur et 1 exemplaire à l'employé

N° de contrat : 2164820.01.0

UNIVERSITÉ DE GENÈVE
RECTORAT

Genève, le 20 septembre 2017

Monsieur
CACIALLI Pietro
Rue des Voisins 8
1205 Genève

Vu l'art. 13 de la loi de l'Université,
vu l'art. 152 du règlement sur le personnel de l'Université de Genève,

L'UNIVERSITE DE GENEVE

DECIDE :

Monsieur Pietro CACIALLI

est nommé post-doctorant

à plein temps

au Département de pathologie et immunologie

du 01.10.2017 au 31.12.2017

Son traitement annuel est fixé à

CHF 82'975.00 (/13) dès le 01.10.2017 (classe 14/2)

Les dispositions des lois et règlements applicables aux membres du personnel de l'Université sont consultables à l'adresse suivante : http://www.unige.ch/collaborateurs/nouveaux/lois.html.

Le Décanat

N° de contrat : 2164620.02.0001

UNIVERSITÉ DE GENÈVE
RECTORAT

Contrat individuel de travail de droit privé
Personnel enseignant

Employeur

Université de Genève

Faculté de médecine

Département de pathologie et immunologie

Employé

Monsieur
Pietro CACIALLI

Rue des Voisins 8
1205 Genève
Suisse

Genève, le 25.09.2017

Ce contrat est conclu aux conditions suivantes :

1. Fonction : post-doctorant
2. Taux d'activité : 100 %
3. Le présent contrat est conclu pour la période du 1er janvier 2018 au 30 novembre 2018

   (le contrat prend fin, même sans résiliation préalable, à la date prévue ci-dessus, sauf reconduction écrite entre les parties, par avenant au présent contrat)
4. Traitement initial Classe : 14 Annuité : 2
   correspondant à un salaire brut annuel de CHF 82'975.00 , soit mensuel de CHF 6'382.70 | X 13 |
5. Période d'essai et/ou autres conditions :
   Compte tenu de vos missions précédentes, vous n'avez pas de temps d'essai.
6. Le statut des membres du corps enseignant rémunérés par des fonds provenant de l'extérieur est régi par le titre V du règlement sur le personnel. Un extrait des dispositions principales applicables du règlement sur le personnel de l'Université ,complété par des dispositions spécifiques, est à disposition au lien suivant :
   http://www.unige.ch/collaborateurs/nouveaux/lois.html
7. Il appartient à l'employé de nous informer immédiatement sur toute modification qui surviendrait dans les renseignements fournis (adresse, situation de famille, etc.)

L'employé déclare avoir pris connaissance des dispositions légales et réglementaires citées qui font partie intégrante du présent engagement.

Date et signature de l'employeur :

25.09.2017

Date et signature de l'employé :

Pietro Cacialli

Distribution : 1 exemplaire à l'employeur et 1 exemplaire à l'employé

N° de contrat : 2164820.03.0001

UNIVERSITÉ DE GENÈVE
RECTORAT

Avenant au contrat individuel de travail de droit privé N° 2164620.03.0001 Personnel enseignant

Employeur

Université de Genève
Faculté de médecine
Département de pathologie et immunologie

Employé

Monsieur
Pietro CACIALLI

Rue des Voisins 8
1205 Genève
Suisse

Genève, le 11.06.2018

Cet avenant est conclu aux conditions suivantes :

1. Fonction : post-doctorant

2. Taux d'activité : 100 %

3. Le présent avenant est conclu pour la période du 1er décembre 2018 au 31 décembre 2018
   (le contrat prend fin, même sans résiliation préalable, à la date prévue ci-dessus, sauf reconduction écrite entre les parties, par avenant au présent contrat)

4. Traitement initial Classe : 14 Annuité : 4
   correspondant à un salaire brut annuel de CHF 85'945.00 , soit mensuel de CHF 6'611.20 | X 13

Date et signature de l'employeur :

Date et signature de l'employé :
25/06/2018

Distribution : 1 exemplaire à l'employeur et 1 exemplaire à l'employé

N° d'avenant : 2164620.03.0003

UNIVERSITÉ
DE GENÈVE
RECTORAT

Genève, le 21 août 2018

Monsieur
CACIALLI Pietro
Rue Jean-Violette 3
1205 Genève

Vu l'art. 13 de la loi de l'Université,
vu l'art. 152 du règlement sur le personnel de l'Université de Genève,

L'UNIVERSITE DE GENEVE

DECIDE :

Monsieur Pietro CACIALLI
est nommé post-doctorant
à plein temps
au Département de pathologie et immunologie
du 01.01.2019 au 31.12.2019

Son traitement annuel est fixé à
CHF 85'945.00 (/13) dès le 01.01.2019 (classe 14/4)

Les dispositions des lois et règlements applicables aux membres du personnel de l'Université sont consultables à l'adresse suivante : http://www.unige.ch/collaborateurs/nouveaux/lois.html.

Le Décanat

N° de contrat : 2164620.04.0001

UNIVERSITÉ DE GENÈVE
FACULTÉ DE MÉDECINE

Genève, le 29 novembre 2019

Monsieur
CACIALLI Pietro
Rue Jean-Violette 3
1205 Genève

Prolongation
Vu l'art. 13 de la loi de l'Université,
vu l'art. 152 du règlement sur le personne] de l'Université de Genève,

L'UNIVERSITE DE GENEVE

DECIDE :

Monsieur Pietro CACIALLI
est prolongé en qualité de post-doctorant à plein temps au Département de pathologie et immunologie
du 01.01.2020 au 30.12.2020

Son traitement annuel est fixé à
CHF 93'958.00 (/13) dès le 01.01.2020 (classe 14/6)

Le Décanat

N° d'avenant : 2372342.08.0002

UNIVERSITÉ
DE GENÈVE
RECTORAT

Genève, le 19 novembre 2020

Monsieur
CACIALLI Pietro
Rue Jean-Violette 3
1205 Genève

Prolongation avec modification

Vu l'art. 13 de la loi de l'Université,
vu l'art. 152 du règlement sur le personnel de l'Université de Genève,

L'UNIVERSITE DE GENEVE

DECIDE :

Monsieur Pietro CACIALLI

est prolongé en qualité de post-doctorant

à plein temps

au Département de pathologie et immunologie

du 01.01.2021 au 30.11.2021

Son traitement annuel est fixé à
CHF 94'569.00 (/13) dès le 01.01.2021 (classe 14/8)

Le Décanat

N° d'avenant :2164620.04.0005

UNIVERSITÉ DE GENÈVE
RECTORAT

Genève, le 5 août 2021

Monsieur
CACIALLI Pietro
Rue Jean-Violette 3
1205 Genève

Vu l'art. 13 de la loi de l'Université,
vu l'art. 152 du règlement sur le personnel de l'Université de Genève,

L'UNIVERSITE DE GENEVE

DECIDE :

Monsieur Pietro CACIALLI

est nommé suppléant maître assistant

à plein temps

au Département de pathologie et immunologie

du 01.10.2021 au 30.09.2022

Son traitement annuel est fixé à
CHF 98'080.00 (/13) dès le 01.10.2021 (classe 17/4)

Les dispositions des lois et règlements applicables aux membres du personnel de l'Université sont consultables à l'adresse suivante : https://www.unige.ch/accueil-infos

Le Décanat

N° de contrat : 2164620.05.0001

UNIVERSITÉ DE GENÈVE

DIVISION DES RESSOURCES HUMAINES

CONDITIONS D'EMPLOI

Madame, Monsieur,

L'Université de Genève se réjouit de vous compter parmi son personnel. Afin de faciliter votre accueil et vos premiers pas dans l'institution, vous trouverez ci-après quelques informations utiles liées à votre nouvel engagement.

Vous êtes un nouveau membre de notre institution ?

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Vous souhaitez garantir le versement de votre salaire ?

- n'oubliez donc pas de retourner dans les meilleurs délais un exemplaire daté et signé de **votre contrat / acte d'engagement**, si demandé, et si cela n'est pas encore réalisé, **de votre cahier des charges** au moyen de l'enveloppe annexée.

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Votre taux d'activité est inférieur à 20% (8 h/semaine) ?

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- assurance maladie : https://www.ch.ch/fr/assurance-maladie-pour-etrangers/
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- cartes multi-services : http://cartes.unige.ch

D'autres informations ?

- consulter le site du Mémento RH https://memento.unige.ch/TM/7

Commission Scientifique de la Fondation

UNIVERSITÉ DE GENÈVE
FACULTÉ DE MÉDECINE

Personelle & Confidentielle

Dr. Pietro CACIALLI
Département de pathologie et immunologie

CMU

Genève, le 05 octobre 2020 CG/cd

Concerne : Appel d'offres 2020, Fondation Gertrude Von Meissner

Cher Collègue,

La Commission scientifique de la Faculté de médecine de l'Université de Genève en charge d'évaluer les demandes de subsides adressées à la Fondation Gertrude von Meissner a étudié votre demonde.

Répondant à l'appel 2020 de la Fondation von Meissner, 24 projets ont été soumis. La Commission scientifique a sélectionné 10 dossiers qui ont été évalués par des experts externs.

Après avoir examiné les deux ropports (dant nous vous remettons copie en annexe), nous avons le plaisir de vous informer que la Fondation Gertrude von Meissner a décidé de soutenir votre projet de recherche intitule:

«The neuropathology of lysosomal storage diseases: insight from a zebrafish model»

en vous accordant la somme de **50'000.00 CHF**.

Les chercheurs sélectionnés par lo Fondation Gertrude von Meissner se verront attribuer leurs subventions de façon officielle par la Faculté de médecine, lors d'une cérémonie publique - le **mardi 03 novembre 2020 à partir de 17H00** - dont les détails vous seront communiqués ultérieurement.

Dans l'intervalle, veuillez recevoir, cher Collègue, mes plus vives félicitations, ainsi que mes meilleures salutations.

Annexe : mentionnée

Cem Gabay
Doyen

DÉCANAT/Fondation Gertrude Von Meissner
CMU - rue Michel-Servet I CH-1211 Genève 4
Té1.022 3795004 | tax0223795002

UNIVERSITÉ
DE GENÈVE

FACULTÉ DE MÉDECINE

La Faculté de Médecine de l'Université de Genève

a l'honneur de décerner à Monsieur Pietro Caciulli

un subside de recherche octroyé par

La Fondation Gertrude von Meissner

pour son projet de recherche portant sur

"The neuropathology of Lysosome Storage Diseases: Insights from a Zebrafish model"

Professeur Michael Mihatsch
Président de la Fondation

Professeur Cem Gabay
Doyen de la Faculté de médecine

Genève, le mardi 03 novembre 2020

Date: 28-04-2020 Applicant: Pietro Cacialli

GERTRUDE VON MEISSNER FOUNDATION

in memory of Annette & Clas Richter

RESEARCH GRANT APPLICATION

1. Applicant (first name, last name): Pietro Cacialli

Degree(s): PhD

Institution name: Faculty of Medicine, Geneva

Institution address: Department of Pathology and Immunology

Phone: +41223795493

E-mail: pietro.cacialli@unige.ch

2. Title of proposal:

The neuropathology of lysosomal storage diseases: insights from a zebrafish model

3. Total budget requested SFR.50'000

Declaration: We the undersigned declare that the information submitted is accurate and complete (to the best of our knowledge) and that we shall accept the Gertrude von Meissner Foundation guidelines, if this application is funded.

Signature of the Principal Investigator:

Pietro Cacialli, PhD

FONDATION ERNEST BONINCHI

Prof. Yves Flückiger
Président
Ligne directe: 022 379 75 13
Yves.Flückiger@unige.ch

Dr. Pietro Cacialli
CMU
Département PATIM,
Rue Michel-Servet 1
1211 Geneve 4

Genève, le 5 mai 2021 FP/mr

Votre requéte à la Fondation Ernest Boninchi concernant le projet << Autophagy: a new therapeutic target to restore synaptic dysfunction in Lysosomal Storage Diseases >>

Monsieur le Docteur,

En ma qualité de Président de la Fondation Ernest BONINCHI et au nom de ses membres, j'ai le plaisir de vous informer que votre requête pour le financement du projet cité en titre a été acceptée par la Fondation.

Ayant relevé le qualités et les perspectives du projet présenté, la Fondation Ernest BONINCHI a décidé de vous attribuer un subside à hauteur de CHF 30'000.--. Cette contribution vous parviendra sous la forme d'une versement unique. A cet effet, je vous remercie d'indiquer à Micheline.Ruetschi@unige.ch les coordonnées du fonds universitaire sur lequel elle doit être versée.

Par ailleurs, la Fondation souhaite être informée de la réalisation de votre projet et de l'utilisation du subside accordé. Elle vous demande donc de bien vouloir lui remettre, au 31 décembre 2022, un rapport scientifique et financier.

En vous souhaitant plein succès dans l'accomplissement de vos activités, je vous prie de croire, Monsieur le Docteur, à l'expression de mes sentiments les meilleurs.

UNIVERSITÀ' DEGLI STUDI DI NAPOLI FEDERICO II

FACOLTA' DI SCIENZE MATEMATICHE FISICHE E NATURALI

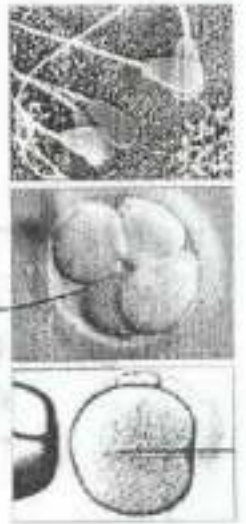
Corso di Perfezionamento
BIOLOGIA e TECNOLOGIE della RIPRODUZIONE ASSISTITA

Si attesta, ai sensi del 3°°comma dell'art. 17 del D.P.R. 10 marzo 1982 n. 162

che il Dott. **Pietro CACIALLI**

nato a Napoli il 28/12/1986 matr. BTRA-234

ha frequentato per 100/100 ore le attività del
Corso Annuale di Perfezionamento in Biologia e Tecnologie della Riproduzione Assistita,
svoltosi presso il Dipartimento di Biologia Strutturale e Funzionale,
superando le opportune verifiche in data odierna.



Napoli 29 Ottobre 2013

Il Direttore del Corso
Prof. Riccardo Talevi

Anno Accademico 2012-2013

ATTESTATO n° **234**

UNIVERSITÀ DEGLI STUDI DI NAPOLI FEDERICO II

N° 405 DEL
REGISTRO RILASCIO
DOCUMENTI.

UFFICIO DOTTORATO, ASSEGNI E BORSE DI STUDIO

Si certifica che il dott. Pietro Cacialli, nato a Napoli il 28.12.1986, ammesso a frequentare il dottorato di ricerca in Organismi modello nella ricerca biomedica e veterinaria 28° ciclo, di durata triennale, presso l'Università degli Studi di Napoli Federico II, ha sostenuto con esito positivo l'esame per il conseguimento del titolo di dottore di ricerca il giorno 20.05.2016, presentando una dissertazione finale dal titolo: "Brain derived neurotrophic factor (BDNF) expression in postnatal and adult zebrafish brain and related changes following mechanical iniury".

Si certfica, inoltre, che al titolo di dottore di ricerca conseguito dal dott. Cacialli è aggiunto il label "Doctor Europaeus" in quanto rispetta le quattro condizioni fissate dalla Confederazione delle Conferenze dei Rettori dell'Unione Europea (oggi EUA - European University Association):

- la dissertazione finale è stata approvata da due docenti appartenenti a due Stati europei diversi: prof. Carmen Solcam dell'Università di Iaşi (Romania) e il prof. Jose Antonio Vega Alvarez dell'Università di Oviedo (Spagna);
- uno dei membri della Commissione giudicatrice è un professore di uno dei due Stati europei diversi: prof. Jorge De Costa Ruiz dell'Università degli Studi di Murcia (Spagna);
- la dissertazione finale è stata presentata e discussa parzialmente in lingua straniera;
- la preparazione della dissertazione finale ha avuto luogo con attività di ricerca svolta per un periodo superiore a tre mesi in uno Stato europeo diverso da quello dove ha sede il dottorato: il dott. Cacialli ha svolto attività di ricerca presso 'Università di Rennes 1 (Francia).

Si rilascia il presente certificato in carta semplice per gli usi consentiti.

Si allega traduzione in lingua inglese del presente certificato.

Ai sensi dell'art. 15 della L. 183/2011 il presente certificato non può essere prodotto agli organi della pubblica amministrazione o ai privati gestori di pubblici servizi.

Napoli, li 30 MAG. 2016

L'IMPIEGATO ADDETTO

UNIVERSITÀ DEGLI STUDI DI NAPOLI FEDERICO II

IL CAPO DELL'UFFICIO
Dott. Concetta Bernardo

UNIVERSITÀ DEGLI STUDI DI NAPOLI FEDERICO II

UNIVERSITY OF NAPLES FEDERICO II

PhD OFFICE

We hereby certify that dr. Pietro Cacialli, born in Naples - Italy – on December 28, 1986 attended the Phd in Models organism in biomedical and veterinary research - 28th cycle – which lasts three years, at the University of Naples Federico II, and passed, with positive result, the exam to achieve the title of PhD on May 20, 2016, presenting the final dissertation: "Brain derived neurotrophic factor (BDNF) expression in postnatal and adult zebrafish brain and related changes following mechanical iniury ".

Moreover, we certify that to the PhD title got by Dr. Cacialli is added the "Doctor Europaeus" label, as it respects the four conditions established by the European University Association:

- the final thesis has been approved by two professors coming from two different European countries: prof. Carmen Solcam of University of Iaşi (Romania) and prof. Jose Antonio Vega Alvarez of University of Oviedo (Spagna);
- one member of the examining board comes from one of two different European countries: prof. Jorge De Costa Ruiz of University of Murcia (Spagna);
- the final thesis has been presented and discussed in foreign language (English);
- the preparation of the final thesis took place with a research period longer than three months spent in a European country different from that of the PhD seat: dr. Cacialli has carried out researches at the University of Rennes 1 (Francia).

We hereby release this certificate for any use that does not legally require an Italian tax stamp.

According to the art. 15 of the L. 183/2011, this certificate can not be issued to the public administration or to private operators of public services.

Naples, 30 MAG. 2016

L'IMPIEGATO ADDETTO

IL CAPO DELL'UFFICIO
Dott.ssa Concetta Bernardo

Ecole Doctorale
Vie-Agro-Santé

UNIVERSITÉ DE RENNES 1

Nathalie Théret
Directrice

ATTESTATION

Je soussignée, Nathalie Théret, directrice de l'école doctorale Vie-Agro-Santé à l'Université de Rennes 1, atteste que Pietro Cacialli a obtenu un prix de recherche d'un montant de 4000 euros.

Fait pour valoir ce que de droit à Rennes, le 19 décembre 2014
La Directrice de l'Ecole Doctorale VAS

Nathalie Théret

UNIVERSITE DE RENNES 1
CAMPUS DE BEAULIEU
263 AV. DU GENERAL LECLERC
CS 74205
35042 RENNES CEDEX

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Reviewer Board Member of MDPI

Dr. Pietro Cacialli

Thank you to review papers for MDPI journals!

Basel, January 2022

Dr. Shu-Kun Lin
Publisher & President

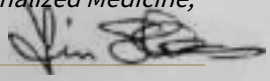
REVIEW CONFIRMATION CERTIFICATE

We are pleased to confirm that

Pietro Cacialli

has reviewed 38 papers for the following MDPI journals in the period 2020–2022:

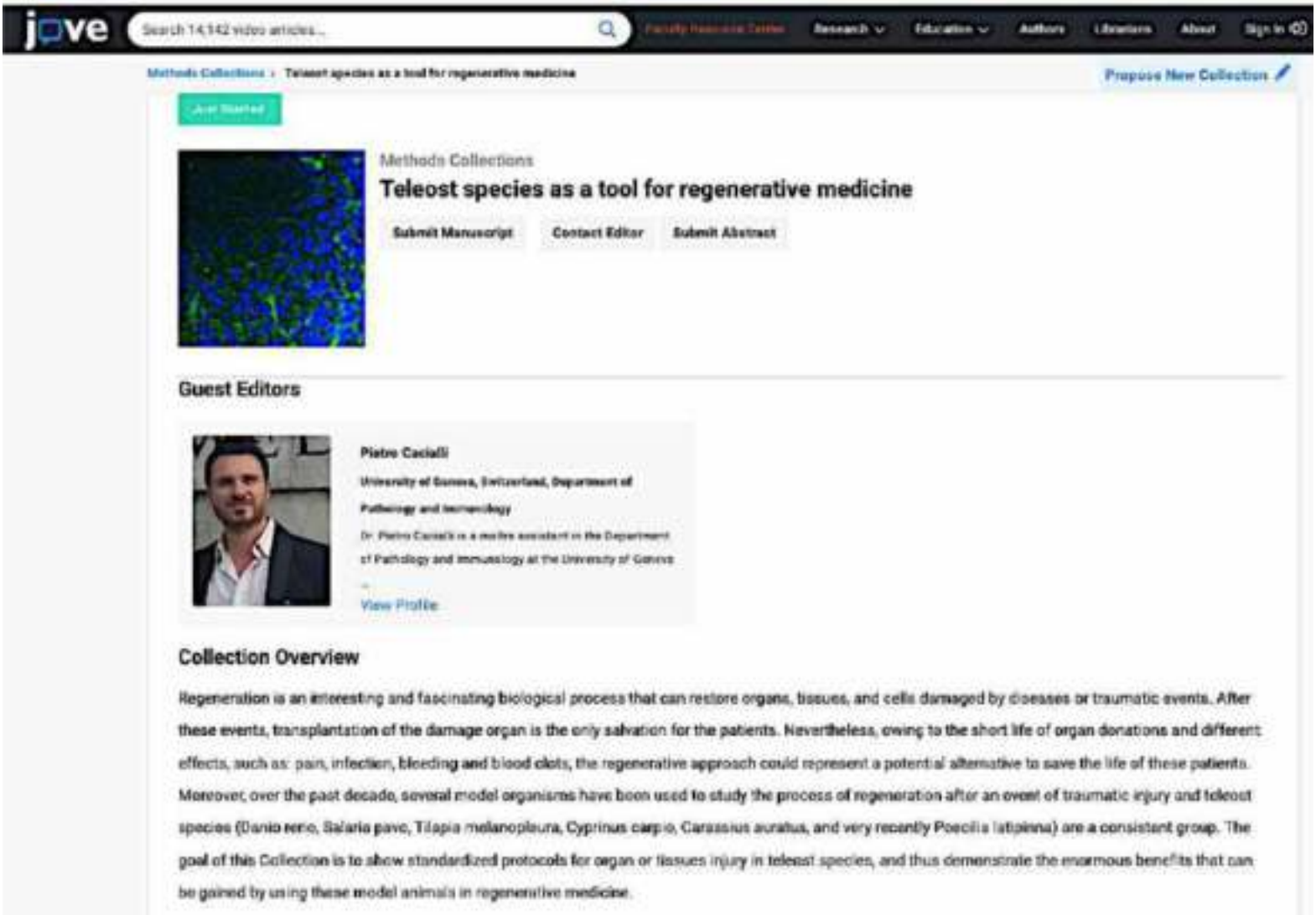
NeuroSci, International Journal of Molecular Sciences, Journal of Clinical Medicine, Biology, Medicines, Journal of Functional Morphology and Kinesiology, Biomolecules, International Journal of Environmental Research and Public Health, Pharmaceuticals, Reports, Sensors, Diagnostics, Journal of Personalized Medicine, Genes, Cells, Brain Sciences



Dr. Shu-Kun Lin, Publisher and
President Basel, 12 January 2022

MDPI

MDPI is a publisher of open access, international, academic journals. We rely on active researchers, highly qualified in their field to provide review reports and support the editorial process. The criteria for selection of reviewers include: holding a doctoral degree or having an equivalent amount of research experience; a national or international reputation in the relevant field; and having made a significant contribution to the field, evidenced by peer-reviewed publications.



https://www.jove.com/methods-collections/982/teleost-species-as-a-tool-for-regenerative-medicine

Program of the 13th Annual Swiss Zebrafish meeting

Thursday April 8th 2021

14.00 **Welcome**

14.10 **Keynote lecture Prof. Corinne Houart**
Center for Developmental Neurobiology, King's College London

Exploring the function of splicing proteins and intron retention in developing neurons

Session 1: Cardiovascular system & Hematopoiesis (moderator Nadia Mercader)

15.00 – 15.15: Pietro Cacialli (University of Geneva)
The cooperation between myeloid and vascular cells favors HSC expansion in the embryonic hematopoietic niche

Talks – abstracts

Session 1: Cardiovascular system & Hematopoiesis

The cooperation between myeloid and vascular cells favors HSC expansion in the embryonic hematopoietic niche

Pietro Cacialli, Julien Y. Bertrand

Department of Pathology and Immunology, School of Medicine, University of Geneva, Switzerland.

During embryonic development, very few hematopoietic stem cells (HSCs) are produced from the hemogenic endothelium, that will be expanded in a very specific niche. This fetal HSC niche comprises a complex and dynamic molecular network of interactions between multiple cell types, including endothelial cells (ECs) and mesenchymal stromal cells. It is known that functional changes in the hematopoietic niche, such as aging, vascular cell re-modelling or inflammation can directly affect HSCs. Among all these inflammatory regulators, the eicosanoid PGE2 has been shown to be very important during embryonic life. However, the precise cellular source of each PGE2 metabolite in the embryo has yet to be cleared. In the present report, we show that all the genes involved in PGE2 synthesis are expressed by different cells of the caudal hematopoietic tissue (CHT) in the embryonic zebrafish, a pattern that seems conserved also in the mouse fetal liver. In the zebrafish CHT, as in mouse fetal liver, we found that neutrophils express high levels of phospholipases, while macrophages express cox1/2 enzymes and endothelial cells (ECs) high levels of ptges. This suggests that each cell type is sequentially necessary to mediate PGE2 synthesis. To measure the impact of myeloid cells, we generated a genetic model of myeloid ablation, which caused a loss of HSCs in the CHT, that could be rescued by supplementing zebrafish embryos with PGE2. Moreover, we identified the role of an important transporter, slco2b1, that mediates the transport of PGE2 across the cell membrane into ECs.

Universität Zürich[UZH]

CERTIFICATE OF ATTENDANCE

Pietro Cacialli

---

has attended the

13th Swiss zebrafish meeting

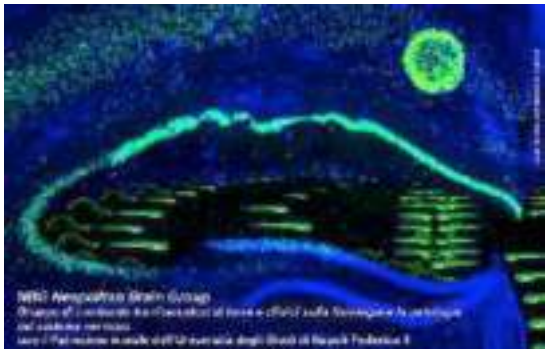
held virtually on April 8th-9th 2021

This meeting is recognized as further training under the Animal Welfare Ordinance for 1.0 day for Animal welfare officers, Study director and involved persons (per decision from the VSKT/ASVC of May 10th 2021).

Zurich, June 10th 2021

For the organizers:

Prof. Dr. Ruxandra Bachmann-Gagescu



Neapolitan Brain Group
Gruppo di confronto tra ricercatori di base e clinici sulla fisiologia e la patologia del sistema nervoso
con il Patrocinio morale dell'Università degli Studi di Napoli Federico II

NERVE GROWTH FACTOR IS EXPRESSED AND STORED IN BRAIN NEURONS OF ADULT ZEBRAFISH
Cacialli Pietro[1,4], Gatta Claudia[1], D'Angelo Livia[1,2], Leggieri Adele[1], Palladino Antonio[3], de Girolamo Paolo[1], Pellegrini Elisabeth[4], Lucini Carla[1]
1.Dip Medicina Veterinaria e produzioni animali, Università di Napoli Federico II, Napoli, Italy; 2. Stazione Zoologica Anton Dohrn, Napoli, Italy; 3. Centro Ricerche Interdipartimentali sui Biomateriali, Università di Napoli Federico II, Naples, Italy; 4. Research Institute in Health, Environment and Occupation, SFR Biosit, University of Rennes 1, Rennes, France
FORMAT PRESENTAZIONE RICHIESTO ☐ Comunicazione orale x Poster
Nerve Growth Factor (NGF), a member of the neurotrophin family, was initially described as neuronal survival and growth factor, but successively has emerged as an active mediator in the central nervous system of mammals. NGF is synthesized as a precursor pro-NGF and is either secreted outside the cells or cleaved intracellularly into mature NGF. Despite the vast literature present in mammals, studies devoted to NGF in the brain of other animal models are scarce. Zebrafish is a teleost fish emerging as model for translational neuroscience research. Genomic organization of zebrafish NGF and mouse NGF are highly similar and zebrafish NGF protein has been reported in a mature and two precursors forms. NGF mRNA was visualized by in situ hybridization on whole brains. NGF protein distribution was assessed on microtomic sections by using an antiserum against NGF which recognizes proNGF in adult zebrafish brain. To characterize NGF positive cells, anti NGF was employed on aromatase B transgenic zebrafish slides (where radial glial cells appeared fluorescent) and by means of double immunolabelling against NGF/PCNA(proliferation marker) and NGF/MAP2 (neuronal marker). NGF mRNA and protein were widely distributed in the brain of adult zebrafish and their pattern of distribution was quite overlapping, both in males and females. MAP2 immunoreactivity was present in the majority of NGF positive cells, throughout the zebrafish brain, while PCNA and aromatase labelled cells were closely intermingled with NGF positive cells. In conclusion, our study demonstrated that several neuronal populations in the zebrafish brain express NGF mRNA and store proNGF.

Associazione Italiana Morfologi Veterinari

ROMA
21-22 Maggio 2015
Palazzina dell'Auditorio
Via della Lungara 230

X CONGRESSO AMV
Roma, 2015

COMITATO ORGANIZZATORE

Adalberto Merighi Presidente
Paolo de Girolamo Vice-presidente
Maddalena Botti Segretario-tesoriere

COMITATO SCIENTIFICO AMV

Emilia Ciriaco
Bruno Cozzi
Cinzia Domeneghini

Gli abstract dei contributi scientifici sono pubblicati in forma preliminare dopo revisione da parte del Comitato Scientifico e prima della pubblicazione definitiva sulla rivista
Annals of Anatomy

2.2 Brain-derived neurotrophic factor (BDNF) and its receptor TrkB, during oocyte development in zebrafish

Cacialli P, *Pellegrini E, Kah O, Castaldo L*

Brain-derived neurotrophic factor (BDNF) is a member of neurotrophin family, whose other components are nerve growth factor (NGF), neurotrophin (NT)3, NT 4/5 and limitedly to fish, NT 6/7. BDNF has been conserved during the vertebrate evolution. The primary amino acid sequences of zebrafish (Danio rerio) and human BDNF are 91% identical. BDNF signaling is transduced by TrkB receptor. In zebrafish there are two genes encoding for TrkB receptor. It is largely known that BDNF and TrkB promotes neuronal growth, differentiation, survival and synaptogenesis. BDNF, such as the other components of neurotrophin family, also acts on non neuronal cell populations. In the ovary, BDNF is involved in mammalian oocyte development, early embryo cleavage and blastocyst formation. To date, no data concerning BDNF and TrkB in teleost fish ovary are available. Thus, this study aims to investigate, by means of immunohistochemistry, the presence and distribution of BDNF and TrkB in the ovary of zebrafish, a teleost fish widely used as vertebrate model. In zebrafish, oocytes undergo five developmental stages. In early stages (I-II) no immunoreactivity to BDNF and TrkB expression was observed. From stage III onward BDNF was detected in the follicle cell layer, and TrkB appeared only in the stage V in thecal cells. These preliminary findings represent the first description of BDNF involvement in teleost fish oocytes development. The occurrence of BDNF in the follicular cells and TrkB in the thecal cells of oocytes stage V suggests a paracrine mode of action.

Associazione Italiana
Morfologi Veterinari

X Congresso Nazionale A.M.V.
Associazione Italiana Morfologi Veterinari

ROMA, 21-22 maggio 2015

Si attesta che

PIETRO CACIALLI

ha partecipato ai lavori
del X Congresso Nazionale
dell'Associazione Italiana Morfologi Veterinari
tenutosi a Roma
il 21 e 22 maggio 2015

Il Presidente A.M.V.
Prof. Adalberto Merighi

Il Segretario Tesoriere A.M.V.
Dott.ssa Maddalena Botti

Mechano-sensing influences morphology and differentiation efficiency during epigenetic conversion of fibroblasts into insulin-producing cells

T.A.L. Brevini [1,*], G. Pennarossa [1], R. Santoro [2], S. Maffei [1], A. Zenobi [1], M. Pesce [2], F. Gandolfi [1]

[1] *Laboratory of Biomedical Embryology – Department of Health, Animal Science and Food Safety and Center for Stem Cell Research, Università degli Studi di Milano, Via Celoria 10, Milan 20133, Italy*
[2] *Laboratorio di Ingegneria Tissutale Cardiovascolare, Centro Cardiologico Monzino-IRCCS, Milan, Italy*

Fibroblasts can be epigenetically converted into insulin-secreting cells (EpiCC), using the epigenetic modifier 5-aza-cytidine (5-aza-CR), followed by a three-step pancreatic induction protocol. Here we investigate if the use of a thin polyacrylamide-based (PAA) gel substrate with soft stiffness may increase the efficiency of differentiation and the acquisition of a more mature phenotype.

Murine skin fibroblasts were plated either on standard plastic dish (group A) or on PAA gel with soft (1 kPa) stiffness (group B). Cells were exposed to 1 μM 5-aza-CR for 18 hours, and then subjected to pancreatic induction for 10 days. At the end of differentiation all EpiCC modified their typical fibroblast elongated shape and acquired an epithelioid morphology. However, while group A cells remained monolayer, group B cells formed three-dimensional spherical structures, reminiscent of in vitro cultured pancreatic islets. Group B cells also showed a significant increase of pancreatic hormone-positivity ($82.83 \pm 6.8\%$ vs. $26.86 \pm 5.8\%$) and became mono-hormonal ($65.33 \pm 2.5\%$). In contrast, 100% of group A cells remained poly-hormonal. Glucose triggered insulin release was significantly higher in B EpiCC (262.57 ± 0.79 mU/μgDNA) than in A (171.22 ± 0.9 mU/μgDNA).

The data presented demonstrate that 3D stiffness regulates cytoskeletal and adhesion mechanics during cell conversion. A soft substrate can drive cell response both at the morphological as well as at the functional level. It increases hormone release and encourages the acquisition of a mono-hormonal mode, which is associated with a mature pancreatic phenotype. This suggests that cell mechano-sensing and biomechanical properties, specifically stiffness-sensing mechanisms, influence cell commitment.

http://dx.doi.org/10.1016/j.aanat.2016.04.005

Brain-derived neurotrophic factor (BDNF) and its receptor TrkB, during oocyte development in zebrafish

P. Cacialli [1,2,*], E. Pellegrini [2], O.O. Kah [2], L. Castaldo [1]

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Brain-derived neurotrophic factor (BDNF) is a member of neurotrophin family, whose other components are nerve growth factor (NGF), neurotrophin (NT) 3, NT 4/5 and limitedly to fish, NT 6/7. BDNF has been conserved during the vertebrate evolution. The primary amino acid sequences of zebrafish (*Danio rerio*) and human BDNF are 91% identical. BDNF signaling is transduced by TrkB receptor. In zebrafish there are two genes encoding for TrkB receptor. It is largely known that BDNF and TrkB promotes neuronal growth, differentiation, survival and synaptogenesis. BDNF, such as the other components of neurotrophin family, also acts on non-neuronal cell populations. In the ovary, BDNF is involved in mammalian oocyte development, early embryo cleavage and blastocyst formation. To date, no data concerning BDNF and TrkB in teleost fish ovary are available. Thus, this study aims to investigate, by means of immunohistochemistry, the presence and distribution of BDNF and TrkB in the ovary of zebrafish, a teleost fish widely used as vertebrate model. In zebrafish, oocytes undergo five developmental stages. In early stages (I-II) no immunoreactivity to BDNF and TrkB expression was observed. From stage III onward BDNF was detected in the follicle cell layer, and TrkB appeared only in the stage V in thecal cells. These preliminary findings represent the first description of BDNF involvement in teleost fish oocytes development. The occurrence of BDNF in the follicular cells and TrkB in the thecal cells of oocytes stage V suggests a paracrine mode of action.

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Programmed cell death in the postnatal cerebellar development of the *Reeler* mouse

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Programmed cell death (PCD) was demonstrated in neurons and glia in normal brain development, plasticity, and aging, but also in neurodegeneration. Autophagy, characterized by cytoplasmic vacuolization and activation of lysosomal hydrolases, and apoptosis, portrayed by chromatin and nuclear condensation, are the two most common forms of PCD. Their underlying intracellular pathways are partly in common and a population of neurons can die following both modalities, according to the type of death-triggering stimulus. Reelin is an extracellular protein necessary for proper neuronal migration and brain lamination. In the mutant *Reeler* mouse, its absence causes neuronal mispositioning, impairment of dendrite outgrowth and reduced numbers of synapses throughout the CNS, with a notable degree of cerebellar hypoplasia that was tentatively related to an increased PCD. We have carried out an ultrastructural analysis on the occurrence and type of postnatal PCD affecting the cerebellar neurons in normal and *Reeler* mice. In the forming cerebellar cortex, PCD took the form of apoptosis or autophagy and mainly affected the granule cells. Numbers of apoptotic neurons were comparable in both mouse strains at P0-P5, while in mutants they increased at P10 and became significantly higher at P15. The number of autophagic neurons in *Reeler* mice increased from birth to P5. It was significantly higher than in controls at P10 and declined thereafter. Therefore cerebellar neurons undergo different types of PCD and a Reelin deficiency affects the type and degree of neuronal death during cerebellar development.

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An improved method for in vitro morphofunctional analysis of dorsal root ganglia in the normal and diabetic mouse

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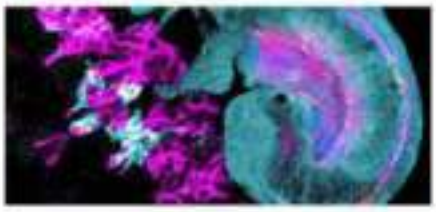
Nociceptive sensory neurons in dorsal root ganglia (DRGs) are the first-order neurons along the pathway that conveys pain to the cerebral cortex. Physiological pain has a protective role, which is



EMBL
European Molecular Biology Laboratory

EMBL Conference: Hematopoietic Stem Cells: From the Embryo to the Aging Organism

Poster 38

The vascular niche protects embryonic HSCs from ROS through IFI30

Authors: Pietro Cacialli, Julien Bertrand

University of Geneva, School of Medicine, Switzerland.

Presenter: Pietro Cacialli

ABSTRACT

In all vertebrates, embryonic hematopoiesis occurs in successive waves, culminating with the emergence of hematopoietic stem cells (HSCs), which will regenerate the blood tissue through adulthood. In zebrafish as in mammals, HSCs initially emerge from the aortic hemogenic endothelium, before they colonize the caudal hematopoietic tissue (CHT), the equivalent of the fetal liver in mammals. The zebrafish CHT is a transient niche where HSCs expand, before they reach their ultimate niche, the kidney. Recent studies showed that HSCs interact with endothelial cells (ECs) in the CHT, and we showed that tfec, a transcription factor from the mitf family, plays an essential role in the niche. We performed RNA sequencing to uncover new tfec target genes that could be involved in the hematopoietic niche. Among the genes up-regulated after tfec overexpression, we identified ifi30 or gilt: Gamma-interferon-inducible lysosomal thiol reductase, an important enzyme for antigen presentation in the context of immunity. By whole mount in situ hybridization, we found that ifi30 is highly expressed in CHT-ECs at the time of HSC colonization, and that this expression depends on tfec. Moreover, ifi30 gain-of-function assays indicate that ifi30 can expand HSCs in the CHT. We are now testing ifi30 loss-of-function and will test for its role in a non-cell autonomous fashion. We conclude that ifi30 is a new target of tfec, and plays an important role in the initial HSC expansion in the CHT. More experiemnts will be necessary to completely unveil this new role of ifi30/gilt in HSC biology.

~~Cours de formation et de perfectionnement pour le personnel spécialisé dans l'expérimentation animale~~ **(Ordonnance du DFI sur les formations à la détention d'animaux et à la manière de les traiter du 5 septembre 2008).**

Organisateurs / *Organizers*: EPFL, UNIL

Attestation de participation / *Certificate of attendance*

Pietro Cacialli

A suivi le 05 septembre 2017 à Lausanne, le symposium mentionné ci-après

Attended on September 5th 2017 in Lausanne the symposium mentioned below

Titre/Titel:

"Swiss Stem Cells Network Meeting 2017"

Symposium de formation continue pour personnes qui executent des expériences sur animaux et pour responsables d'expériences sur animaux / *Continuous education for experimenters and persons conducting animal experimentation*

Ce symposium compte comme ½ journée de formation continue
This event has been validated as ½ day of continuous education

Le symposium mentionné ci-dessus a été accrédité par l'Association Suisse des Vétérinaires Cantonaux (ASVC) - courrier du Dr. Walter Zeller en date du 8 septembre 2017

This event has been accredited by the « association suisse des vétérinaires cantonaux (ASVC) » – letter from Dr. Walter Zeller, september 8th 2017.

Lausanne, 08.09.2017

Dr. Laure Seriot
Présidente du Resal

Dr Fabienne Chabaud
Resal coordinator

NERVE GROWTH FACTOR IS EXPRESSED AND STORED IN BRAIN NEURONS OF ADULT ZEBRAFISH

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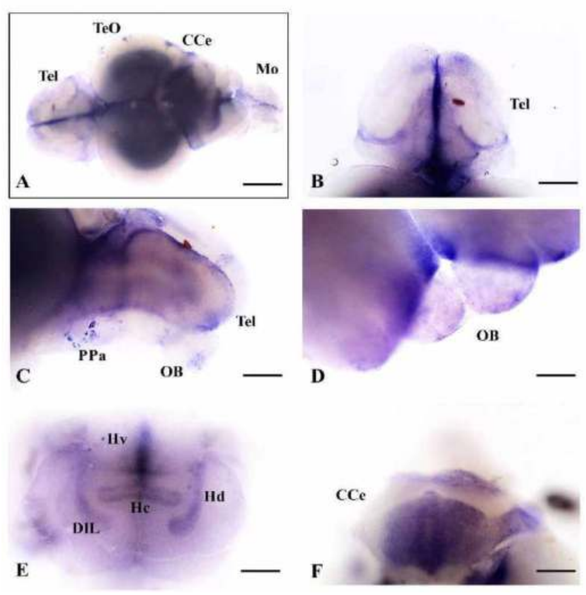
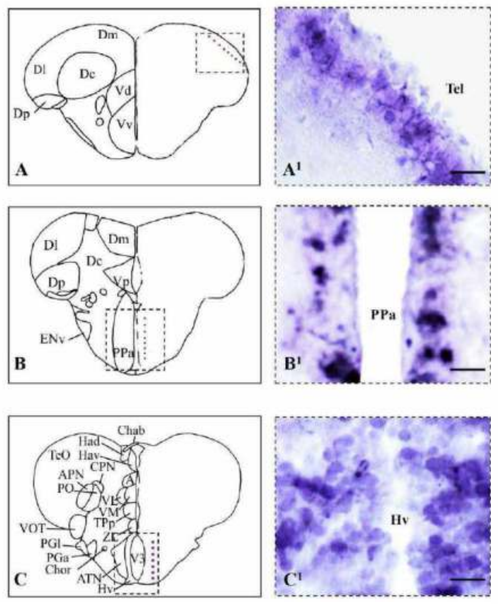
Nerve Growth Factor (NGF), a member of the neurotrophin family, was initially described as neuronal survival and growth factor, but successively has emerged as active mediator in the central nervous system of mammals. NGF is synthesized as precursor pro-NGF and is either secreted outside the cells or cleaved intracellularly into mature NGF. Despite the vast literature present in mammals, studies devoted to NGF in the brain of other animal models are scarce. Zebrafish is a teleost fish emerging as model for translational neuroscience research. *Ngf* organization is highly similar in zebrafish and mouse. Besides to mature NGF protein, two precursors are known in zebrafish.

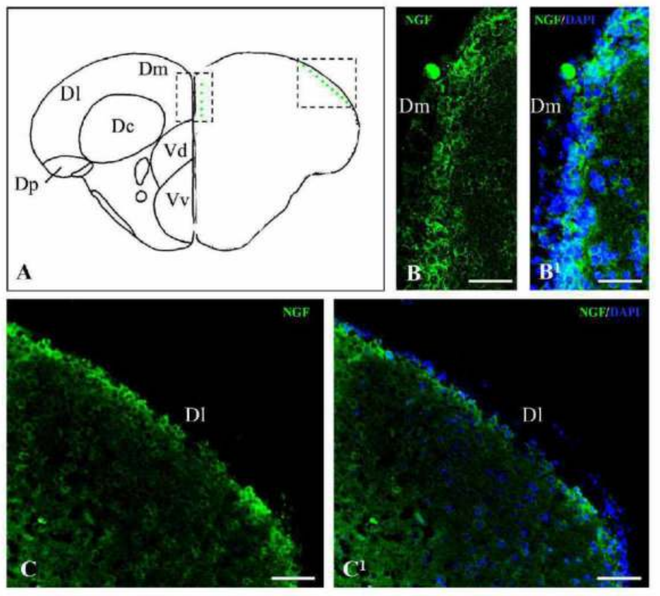
NGF mRNA was visualized by in situ hybridization on whole brains. NGF protein distribution was assessed on microtomic sections by using an antiserum against NGF which recognizes proNGF. To characterize NGF positive cells, anti NGF was employed on aromatase B transgenic zebrafish slides (where radial glial cells appeared fluorescent) and by means of double immunolabelling against NGF/PCNA (proliferation marker) and NGF/MAP2 (mature neuronal marker).



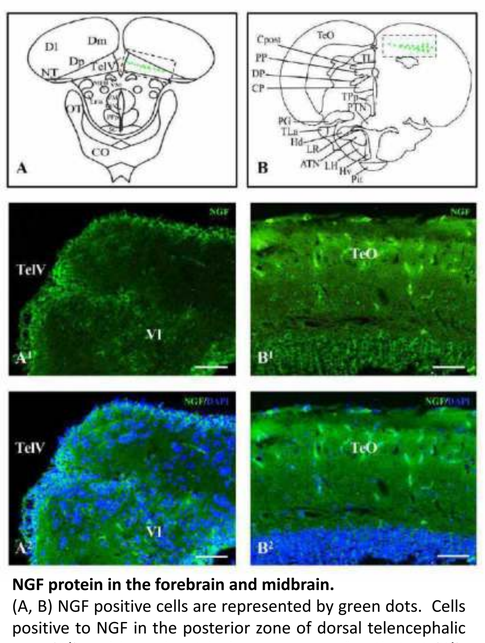
NGF mRNA in whole mount-brain of adult zebrafish.
NGF mRNA distribution in whole mount brain (A); telencephalon (B); preoptic area and olfactory bulbs (C, D); hypothalamus (E), cerebellum (F).



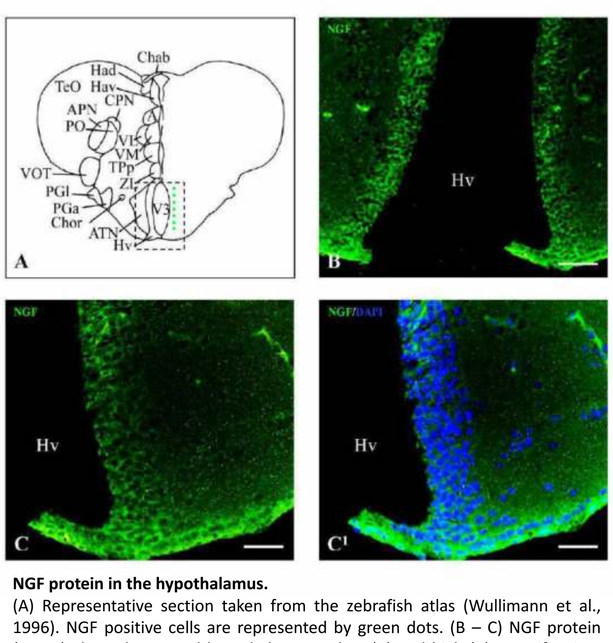
NGF mRNA in cross-section of adult zebrafish brain.
(A – C) NGF positive cells are represented by blue dots. (A[1] – C[1]) NGF positive cells in the dorsal part of telencephalon (A[1]), in the preoptic area (B[1]) and along the ventral part of hypothalamus (C[1]).



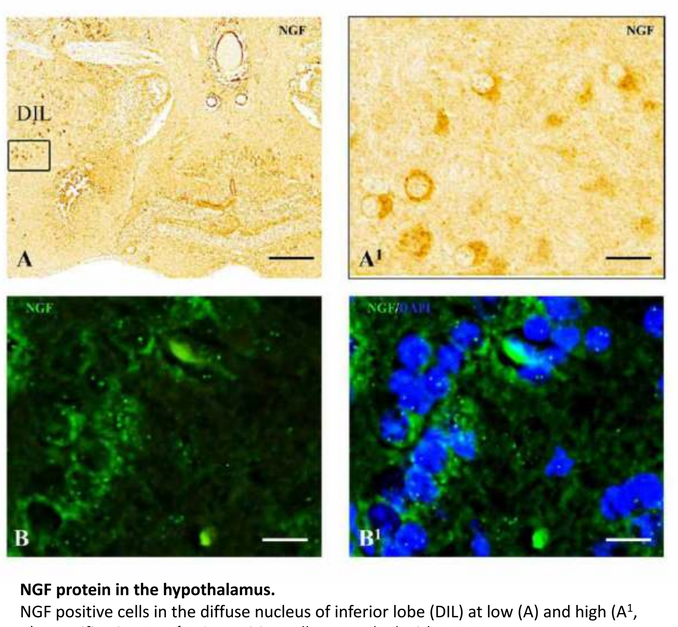
NGF protein in the telencephalon.
(A) NGF positive cells are represented by green dots. (B - C) Cells positive to NGF in the medial (B) and lateral (C) zone of telencephalon. (B[1], C[1]) NGF positive cells co-marked with DAPI.



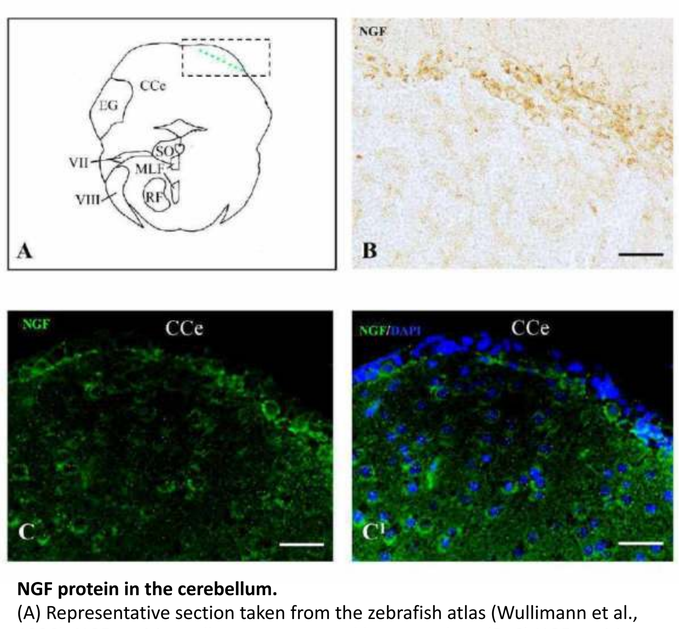
NGF protein in the forebrain and midbrain.
(A, B) NGF positive cells are represented by green dots. Cells positive to NGF in the posterior zone of dorsal telencephalic area (A[1]) and in periventricular gray zone of optic tect (B[1]). (A[2], B[2]) NGF positive cells co-marked with DAPI.



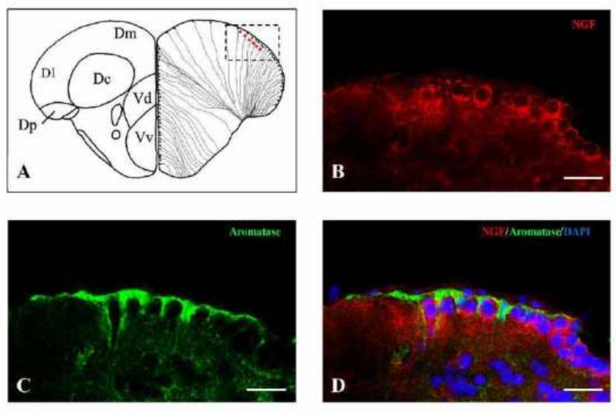
NGF protein in the hypothalamus.
(A) Representative section taken from the zebrafish atlas (Wullimann et al., 1996). NGF positive cells are represented by green dots. (B – C) NGF protein (green) along the ventral hypothalamus at low (B) and high (C) magnification. (C[1]) NGF positive cells co-marked with DAPI.



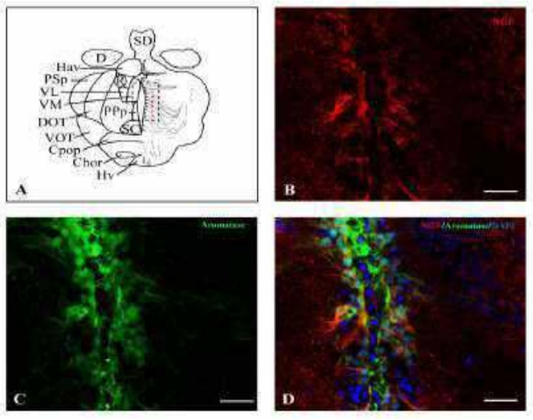
NGF protein in the hypothalamus.
NGF positive cells in the diffuse nucleus of inferior lobe (DIL) at low (A) and high (A[1], B) magnification. In B[1] NGF positive cells co-marked with DAPI.



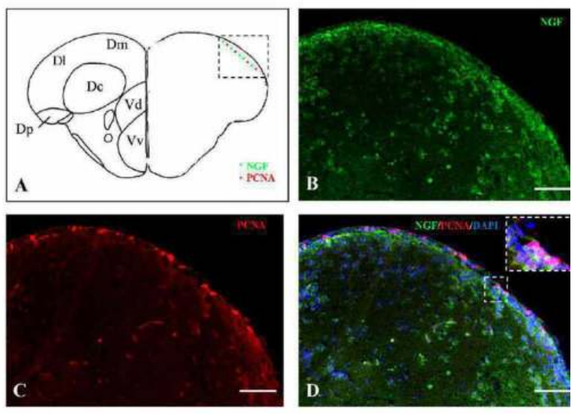
NGF protein in the cerebellum.
(A) Representative section taken from the zebrafish atlas (Wullimann et al., 1996). NGF positive cells are represented by green dots. (B, C) NGF positive cells in the Purkinije layer of cerebellum. In C[2] NGF positive cells co-marked with DAPI.



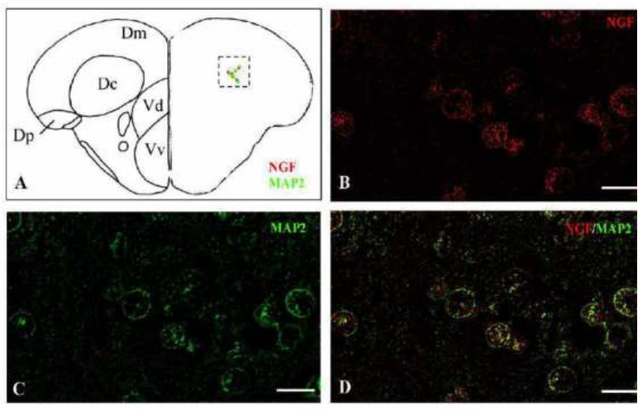
Immunohistochemical characterization of NGF positive
(A) NGF positive cells are represented by red dots and Aromatase B is represented by black dots with thin lines indicating radial glia cytoplasmic processes. (B – D) Double staining for NGF (red) (B) and Aromatase-B (green) (C) on cross-sections through the telencephalon, merge with DAPI (D).



NGF protein is not preferentially detected in radial glial cells. (A) representative sections taken from the zebrafish atlas (Wullimann et al., 1996), red dots represent NGF protein distribution along the diencephalic ventricles and black dots with thin line indicating radial glia cells. (B) NGF positive cells in red, (C) aromatase B, (D) merge with DAPI.



Immunohistochemical characterization of NGF positive cells.
(A) NGF positive cells are represented by green dots and PCNA positive cells by red dots. (B – D) Double staining for NGF (green) (B), PCNA(red) (C), merge with DAPI and high-magnification of a zoom area (D) on cross-sections through the telencephalon.



Immunohistochemical characterization of NGF positive cells.
(A) NGF positive cells are represented by red dots and MAP2 positive cells by green dots. (B – D) Double staining for NGF (red) (B), MAP2 (green) (C) and merge (D) on cross-sections through the telencephalon.

NGF mRNA and protein were widely distributed in the brain of adult zebrafish and their distribution pattern was quite overlapping, both in males and females. MAP2 immunoreactivity was present in the majority of NGF positive cells, throughout the zebrafish brain. PCNA and aromatase B cells were not positive to NGF, but they were closely intermingled with NGF cells. In conclusion, our study demonstrated that mature neurons in the zebrafish brain express NGF mRNA and store proNGF.

Myeloid and endothelial cells cooperate to promote hematopoietic stem cells expansion in the fetal niche

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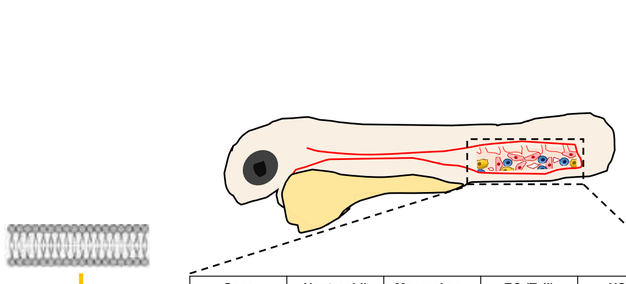
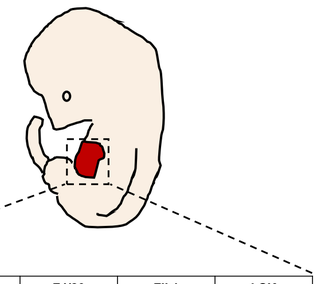
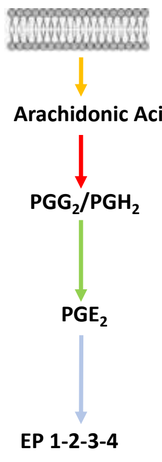
ABSTRACT

During embryonic development, very few hematopoietic stem cells (HSCs) are produced from the hemogenic endothelium, that will be expanded in a very specific niche. This fetal HSC niche comprises a complex and dynamic molecular network of interactions between multiple cell types, including endothelial cells (ECs) and mesenchymal stromal cells. It is known that functional changes in the hematopoietic niche, such as aging, vascular cell re-modelling or inflammation can directly affect HSCs. Among all these inflammatory regulators, the eicosanoid PGE2 has been shown to be very important during embryonic life. However, the precise cellular source of each PGE2 metabolite in the embryo has yet to be cleared. In the present report, we show that all the genes involved in PGE2 synthesis are expressed by different cells of the caudal hematopoietic tissue (CHT) in the embryonic zebrafish, a pattern that seems conserved also in the mouse fetal liver. In the zebrafish CHT, as in mouse fetal liver, we found that neutrophils express high levels of phospholipases, while macrophages express cox1/2 enzymes and endothelial cells (ECs) high levels of ptges. This suggests that each cell type is sequentially necessary to mediate PGE2 synthesis. To measure the impact of myeloid cells, we generated a genetic model of myeloid ablation, which caused a loss of HSCs in the CHT, that could be rescued by supplementing zebrafish embryos with PGE2. Moreover, we identified the role of an important transporter, slco2b1, that mediates the transport of PGH2 across the cell membrane into ECs.

qPCR screening of Prostaglandin metabolic enzymes





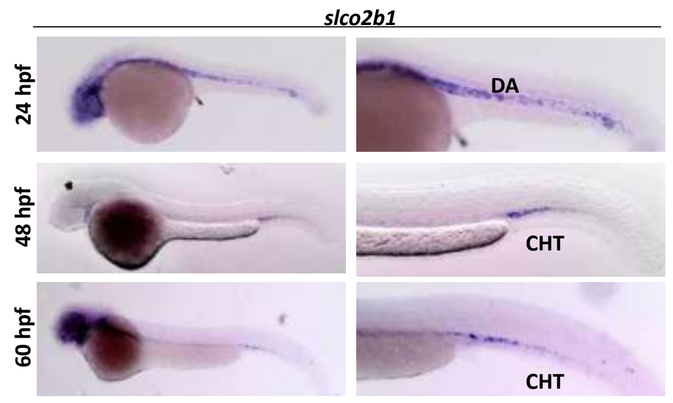


Gene	Neutrophil	Macrophage	EC (Tail)	HSPC
pla2g4aa	++++	+	+	-
pla2g4ab	++++	+	-	-
cox1	-	++++	+	-
cox2a	+	++++	+	-
cox2b	-	++++	+	-
ptges3a	+	-	+++	-
ptges3b	-	+	++++	-
slco2b1	-	-	++++	-
abcc4	-	-	++++	-
ptger1a	-	-	-	++++
ptger1b	++	-	-	++++
ptger2a	-	-	-	++++
ptger3	++++	-	-	+
ptger4a	++	-	-	+++

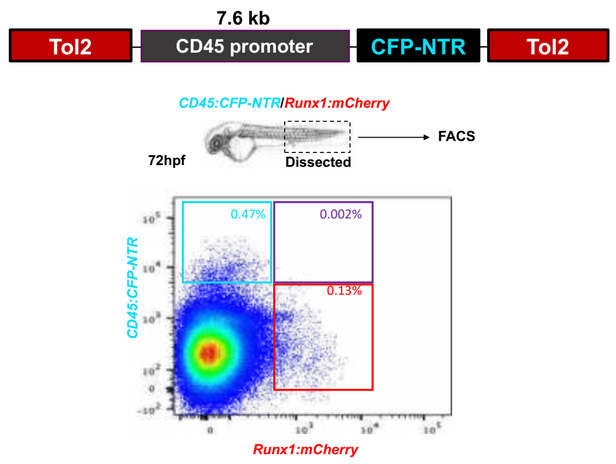
Gene	Gr-1	F4/80	Flk1	LSK
Pla2g4a	++	+	+	+
Pla2g4b	++	-	+	+
Pla2g4c	-	++	+	-
Cox1	-	+++	+	-
Cox2	-	++++	-	-
Slco2b1	+	-	++++	+
Ptges3	+++	+	++++	-
Abcc4	-	++	+	-
Ptger1	+	-	-	++
Ptger2	-	+++	-	-
Ptger3	-	++	+	++++
Ptger4	-	++	-	++

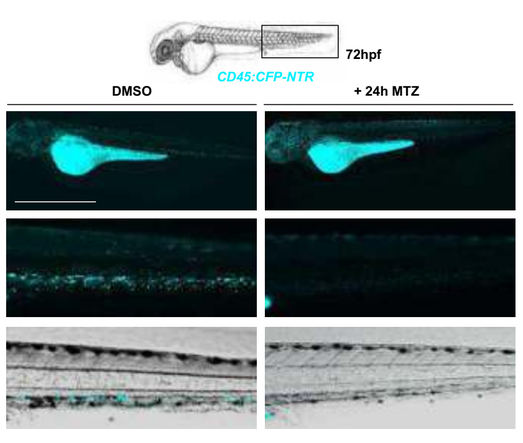
Slco2b1 in the hematopoietic niches

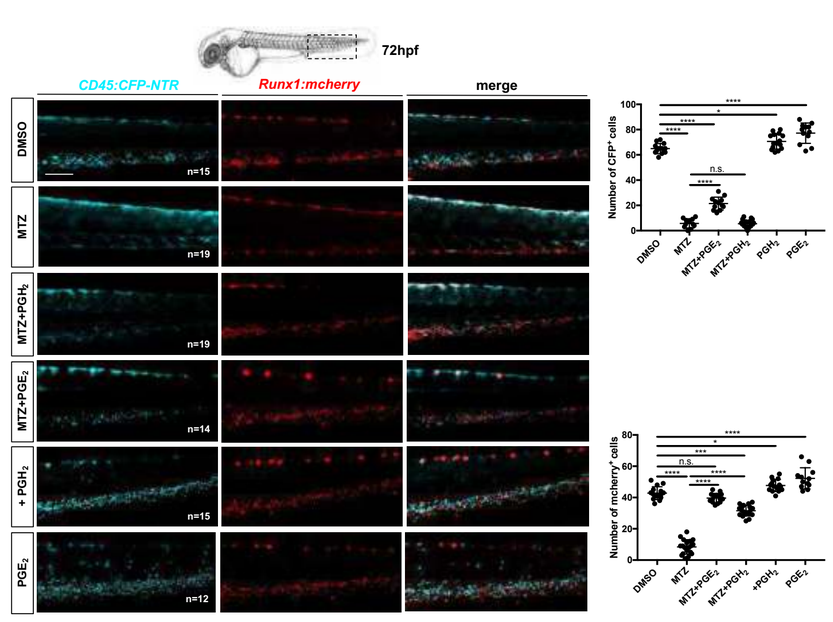
SLCO2B1 transporter present 12-transmembrane domain, a signature sequence, a junction between the third extracellular loop and transmembrane domain 6. Conserved cysteine residues are localized to the fifth extracellular loop. A mutation of these conserved cysteine inhibit the function of the transporter. We found *slco2b1* expressed in the Dorsal Aorta (DA) and caudal hematopoietic tissue (CHT).

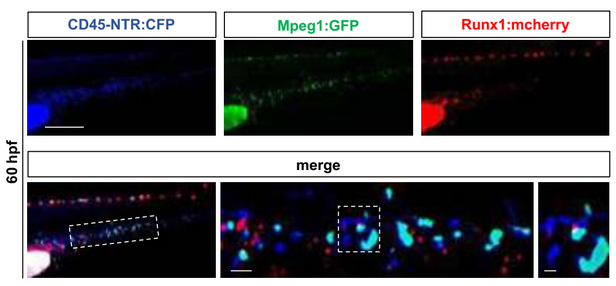


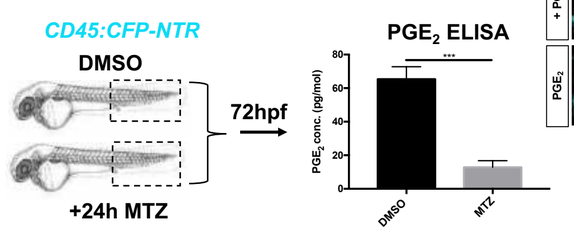
The specific ablation of myeloid cell decreases the number of HSCs in the CHT



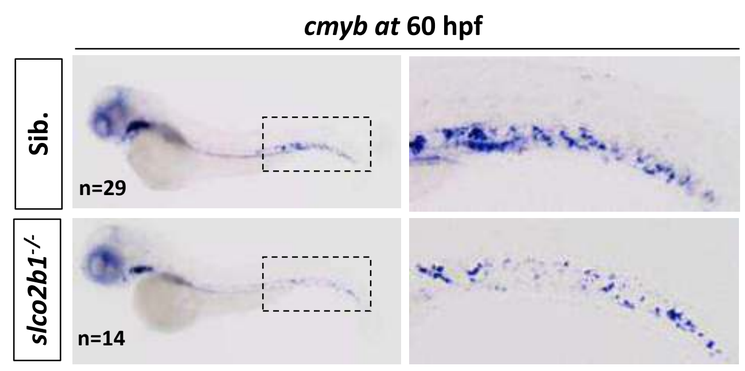


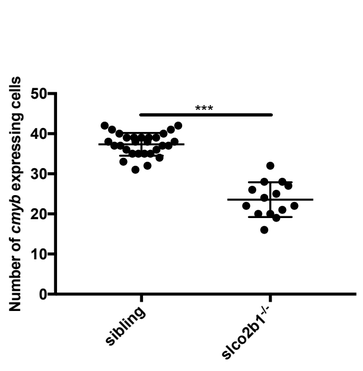


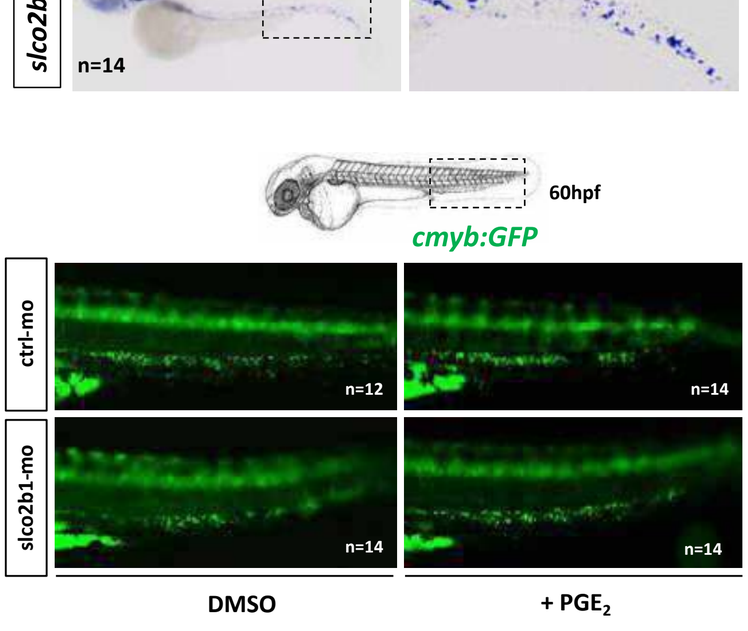


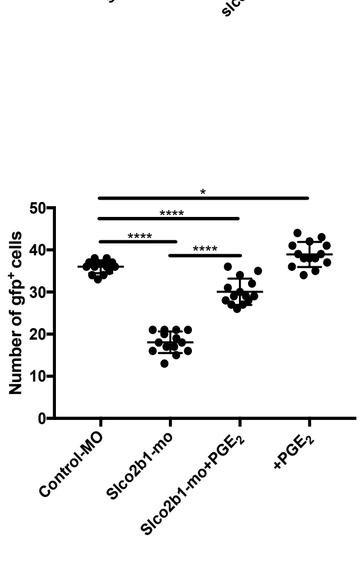


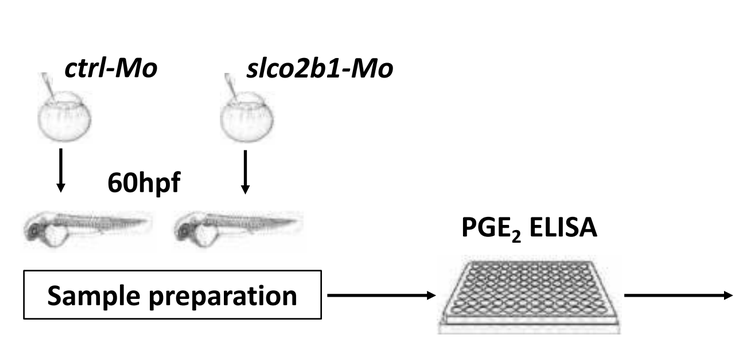
Slco2b1-deficient embryo shows a decrease of HSPCs caused by a reduced level of PGE_2

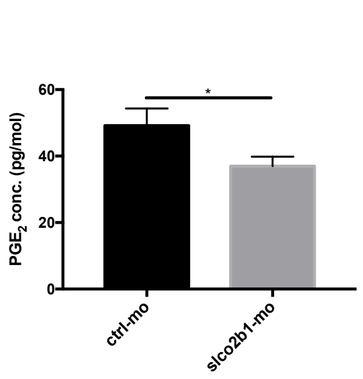


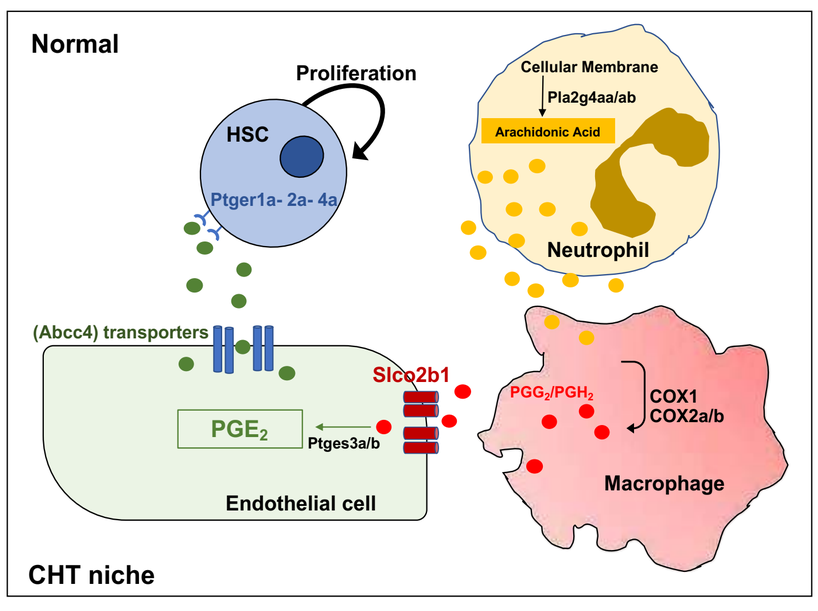


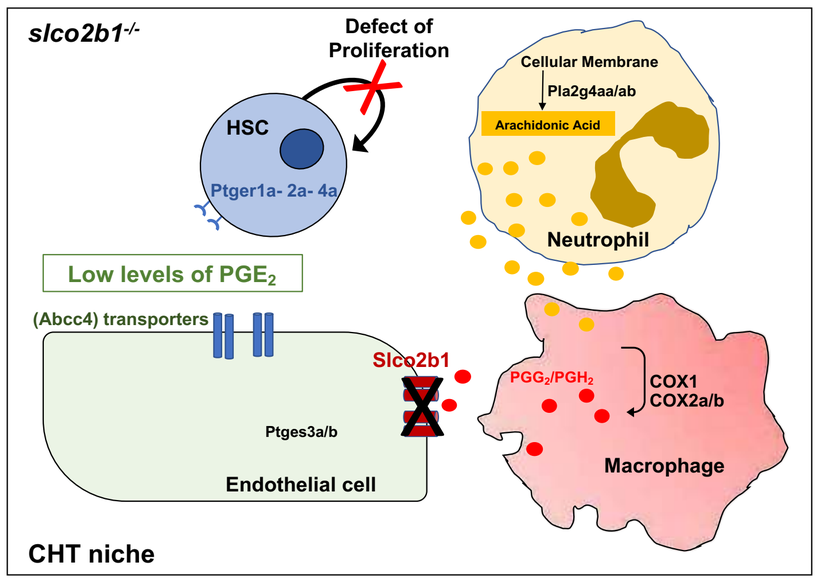












UNIVERSITÉ DE GENÈVE

Brain derived neurotrophic factor in the ovary of zebrafish

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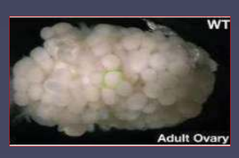
2 Team NEED, IRSET, IFR 140, Rennes, France

INTRODUCTION

Brain-derived neurotrophic factor (BDNF) is a member of neurotrophin family. BDNF is a conserved molecule during the vertebrates evolution. It has been demonstrated that the primary amino acid sequences of zebrafish (*Danio rerio*) and human BDNF are 91% identical. It is largely known that BDNF in the nervous system promotes neuronal growth, differentiation, survival and synaptogenesis. BDNF also acts on several organs. In the ovary of mammals and birds, BDNF is involved in oocyte and early embryo development. However, to date, there are no data concerning BDNF in teleost fish ovary. Thus, this study aims at investigating the presence and distribution of BDNF in the ovary of zebrafish.

MATERIALS AND METHODS

Adult female zebrafish were anesthetized using 0,033% aminobenzoic acid-ethyl-methyl-ester (MS222, Sigma, St. Louis, MO). The ovaries were dissected and homogenized to extract RNA for qRT-PCR, or fixed for one day in paraformaldeyde 4% and, after dehydration, included in paraffin and sectioned at 7mμ. The sections were used for hematoxylin-eosin, in situ hybridization and immunohistochemical stainings.



HISTOLOGICAL ANALYSIS

The different stages of the oocytes, observed in sections stained by hematoxylin-eosin, have been classified following:

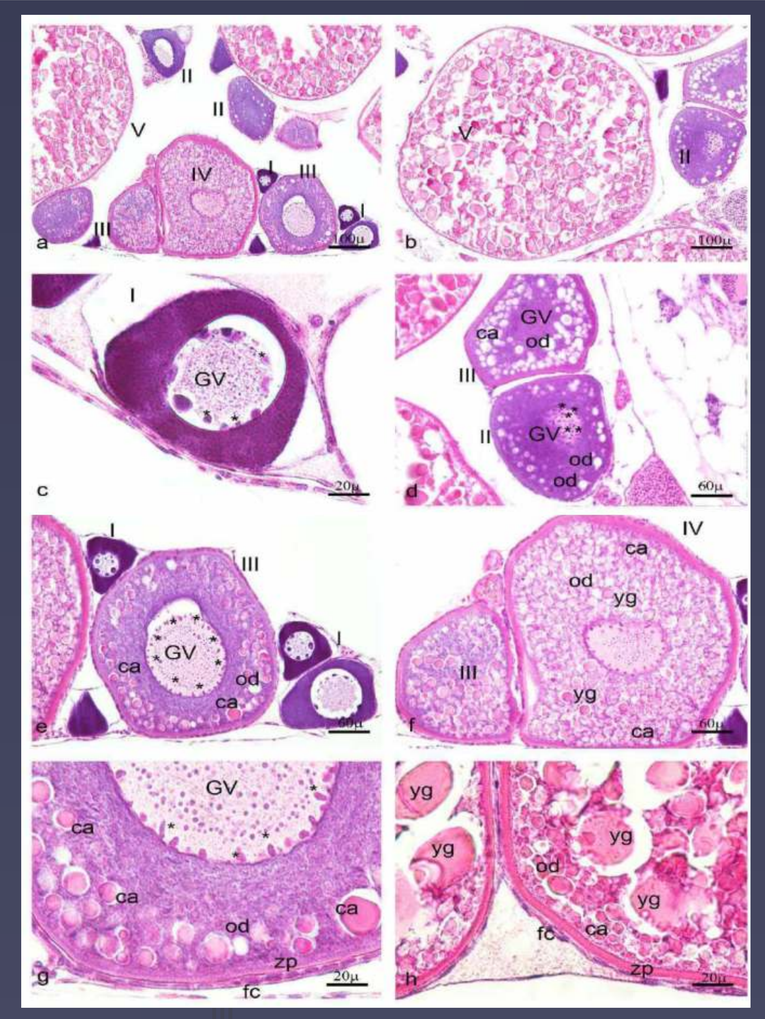
stage I. Oogonia (c) characterized by large euchromatic germinal vescicle (GV), several nucleoli (*) peripherically located.

stage II. Oocyte (d) during primary growth (d) characterized by an increase of nucleoli in GV, and in ooplasma were present oil droplets (od) around the GV.

stage III. Oocyte (e-g) characterized by numerous nucleoli at the periphery of GV, and numerous od and cortical alveoli (ca). The oocyte is enveloped by zona pellucida (zp) and a single layer of follicular cells (fc).

stage IV. Oocyte (f) characterized by a significant increase of oil droplets and cortical alveoli and appearing of yolk globules (yg). The zp appeared thicker than previous stage.

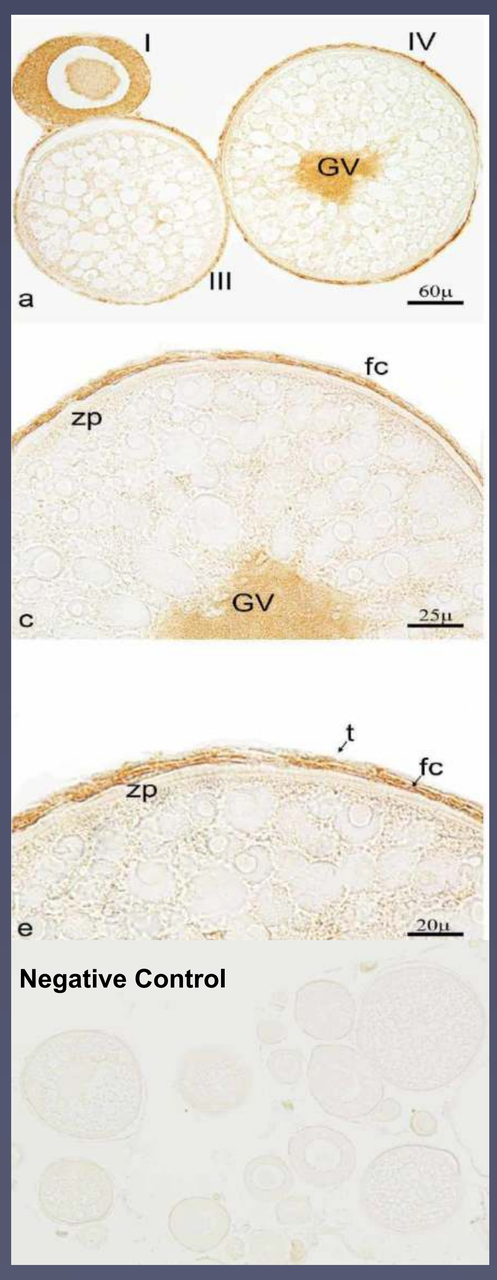
stage V. Oocyte (b-h) characterized by a significant increase of number and size of the yg. Significant increase in the thickness of the zp and appearance of thecal layer.



RESULTS

The BDNF antibody was a rabbit polyclonal against human internal region (N-20, Santa Cruz Biotechnology; dilution 1:500). Immunohistochemical analysis showed that BDNF immunoreactvity was present within follicle cell layer (fc), around the zona pellucida (zp), during different stages of oocyte development.

The specificity of the immunohistochemical reactions was checked as follows: substitution of the primary antibody by PBS; and treatment of the primary antibody with correlated antigen, the peptide sc-546P Santa Cruz Biotechnology (100 μg/ml in the final dilution).

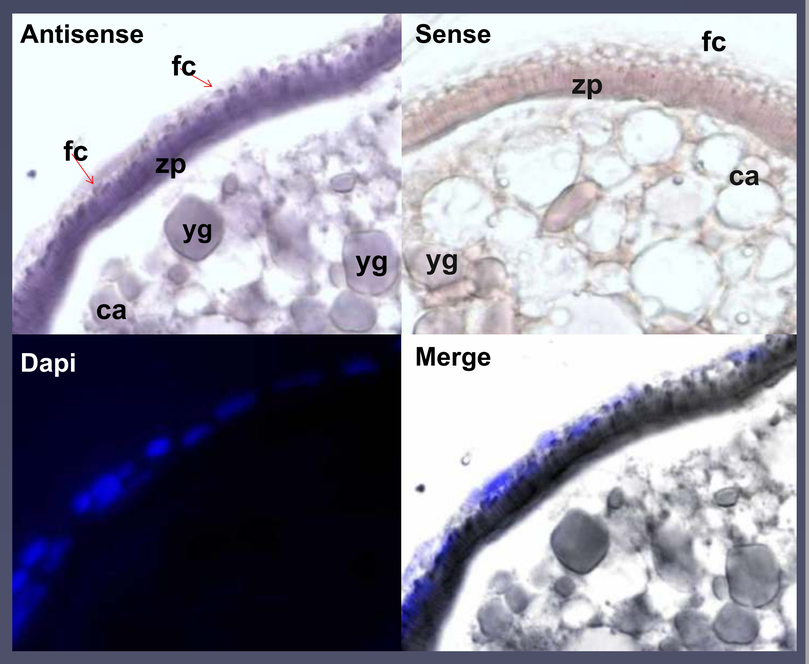


Negative Control

RESULTS

In situ hybridization analysis showed that mRNA BDNF was expressed in the follicle cells (fc) layer around the zona pellucida (zp) of the oocytes.

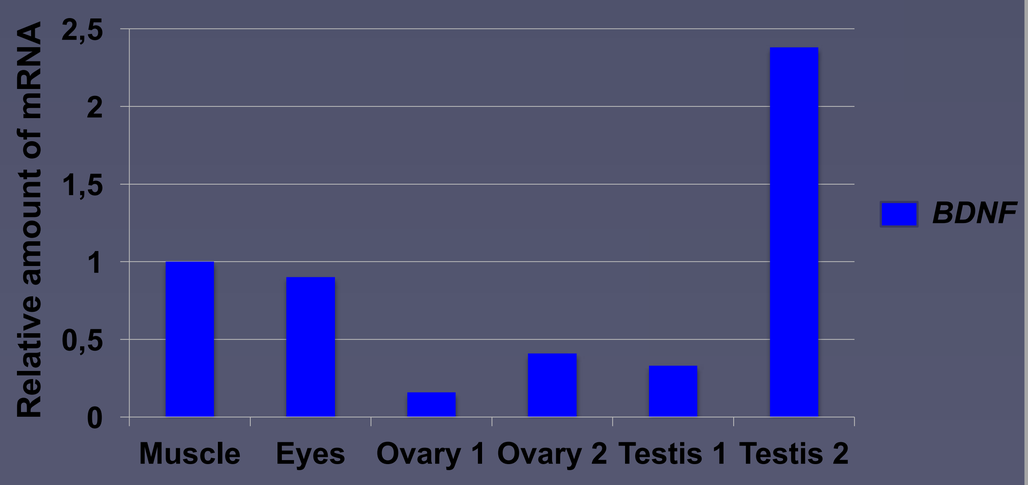
Digoxigenin-labeled sense and antisense riboprobes for BDNF were produced using a template linearized with Not1 and transcribed using SP6 RNA polymerase for the sense probe, or linearized with EcoRI and transcribed using T7 RNA polymerase for the antisense probe.



RESULTS

Quantifying of BDNF expression using qRT-PCR.

We calculated different expressions in various tissues.



CONCLUSION

These preliminary findings demonstrate that protein and transcript of BDNF are localized in the follicular cells at different stages of development. Thus, they suggest an involvement of this neurotrophin in zebrafish oocyte development.

Supported by the mobility grant of Doctoral School VAS (Vie-Agro-Santè), University of Rennes 1

Brain derived neurotrophic factor in the ovary of zebrafish

Pietro Cacialli1,2, Livia D'angelo1, Paolo De Girolamo1, Carla Lucini1, Elisabeth Pellegrini2, Olivier Kah2 , Luciana Castaldo1

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Brain derived neurotrophic factor (BDNF) is a member of the neurotrophin family, whose other components are nerve growth factor (NGF), neurotrophin (NT) 3, NT 4/5 and NT 6/7. BDNF has been highly conserved molecule during the vertebrate evolution. It has been demonstrated that the DNA-deduced amino-acid sequence of the processed mature BDNF of the teleost fish *Xiphophorus maculatum* shows 90% identity with the mouse sequence. Also, the primary amino acid sequences of zebrafish (*Danio rerio*) and human BDNF are 91% identical. It is largely known that BDNF in the nervous system promotes neuronal growth, differentiation, survival and synaptogenesis. However, BDNF, similar to other neurotrophins, acts on several peripheral organs. In the ovary, BDNF is involved in mammalian oocyte development, early embryo cleavage and blastocyst formation. However, to date, there are no data concerning BDNF in teleost fish ovary. Thus, this study aims to investigate the presence and distribution of BDNF in the ovary of zebrafish, a teleost fish widely used as vertebrate model. The identification of the different stages of oocytes was carried out by morphological basis and BDNF was investigated by immunohistochemistry, *in situ* hybridization and qPCR. Our results showed BDNF expression in follicle cell layer in later stage. In conclusion, these preliminary findings demonstrated that BDNF is synthesized and stored in the ovary of zebrafish, suggesting an involvement of this neurotrophin in oocyte development.

Zebrafish gamma interferon-inducible lysosomal thiol reductase (*ifi30*), a new target of the transcription factor *tfec*, expands hematopoietic stem cells.

Pietro Cacialli, Julien Y. Bertrand

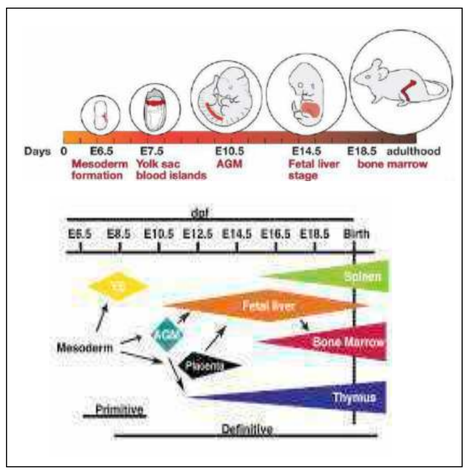
University of Geneva, School of Medicine, Department of Pathology and Immunology

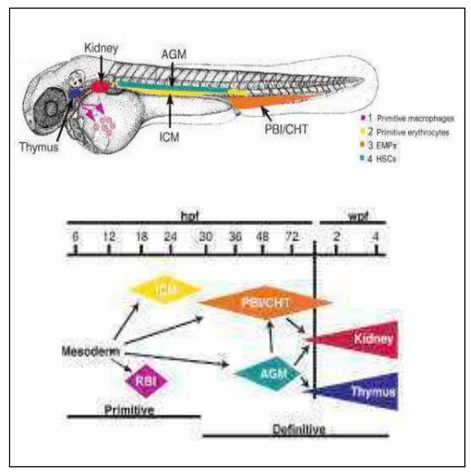
Research group of hemato-vascular development in vertebrates

ABSTRACT

In all vertebrates, embryonic hematopoiesis occurs in successive waves, culminating with the emergence of hematopoietic stem cells (HSCs), which will regenerate the blood tissue through adulthood. In zebrafish as in mammals, HSCs initially emerge from the aortic hemogenic endothelium, before they colonize the caudal hematopoietic tissue (CHT), the equivalent of the fetal liver in mammals. The zebrafish CHT is a transient niche where HSCs expand, before they reach their ultimate niche, the kidney. Recent studies showed that HSCs interact with endothelial cells (ECs) in the CHT, and we showed that tfec, a transcription factor from the mitf family, plays an essential role in the niche. We performed RNA sequencing to uncover new *tfec* target genes that could be involved in the hematopoietic niche. Among the genes up-regulated after *tfec* overexpression, we identified *ifi30* or *gilt*: Gamma-interferon-inducible lysosomal thiol reductase, an important enzyme for antigen presentation in the context of immunity. By whole mount in situ hybridization, we found that *ifi30* is highly expressed in CHT-ECs at the time of HSC colonization, and that this expression depends on *tfec*. Moreover, *ifi30* gain-of-function assays indicate that *ifi30* can expand HSCs in the CHT. We are now testing *ifi30* loss-of-function and will test for its role in a non-cell autonomous fashion. We conclude that *ifi30* is a new target of *tfec*, and plays an important role in the initial HSC expansion in the CHT. More experiments will be necessary to completely unveil this new role of *ifi30/gilt* in HSC biology.

Hematopoietic Development

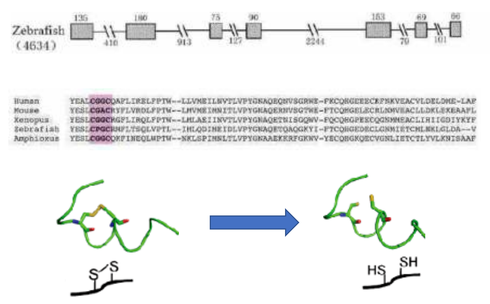




In mouse, primitive hematopoiesis initiates in the yolk sac, producing primitive macrophages and erythroid cells. Later, definitive EMPs emerge in the yolk sac. HSCs are specified in the aorta, gonad, and mesonephros AGM region. Zebrafish hematopoiesis is similar: primitive macrophages arise from cephalic mesoderm and migrate onto the yolk ball. Primitive erythrocytes develop in the intermediate cell mass. The first definitive progenitors are EMPs, which develop in the PBI. Later, HSCs arise in the AGM region. At 2 to 6 days post fertilization (dpf), definitive hematopoietic precursors enter the circulation, colonize, and expand in the caudal hematopoietic tissue, which is equivalent to mouse fetal liver. In fish, hematopoiesis then shifts to the kidney and thymus. In the mouse, hematopoiesis shifts from fetal liver to bone marrow.

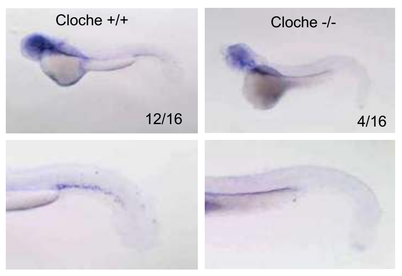
Stachura and Traver, Methods in Cell Biology 2016

ifi30



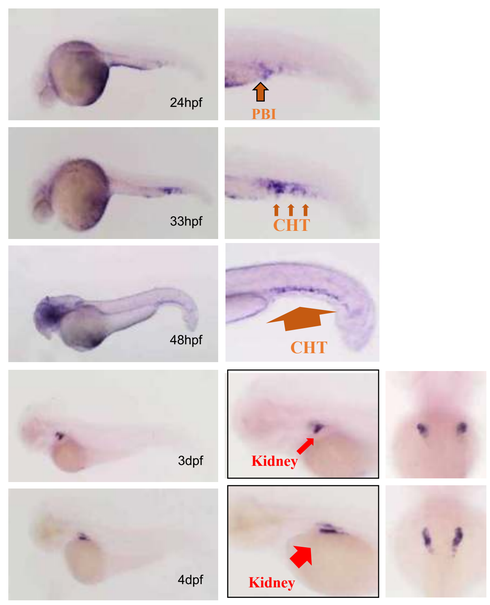
Gamma-interferon-inducible lysosomal thiol reductase (IFI30 or Gilt), functions in MHC class II-restricted antigen processing and MHC class I-restricted cross-presentation by reducing disulfide bonds of endocytosed proteins and facilitating their unfolding and optimal degradation.

West and Cresswell Curr. Opin. Immunology 2013

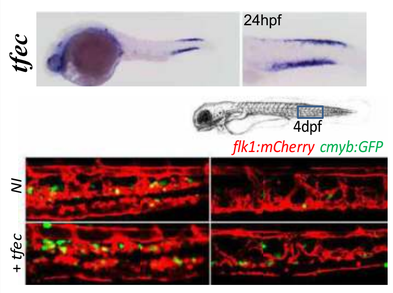


Ifi30 expression is absent in cloche mutant at 48 hpf

Ifi30 expression in zebrafish



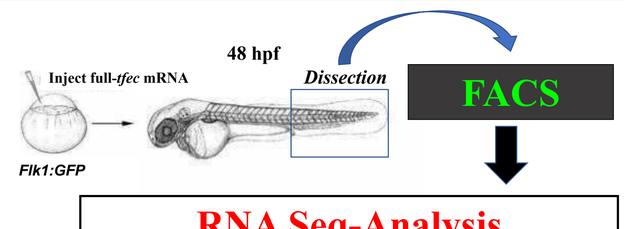
The transcription factor *tfec*



***tfec* overexpression augments the number and proliferation (G2/M phase) of HSPCs in the CHT.**

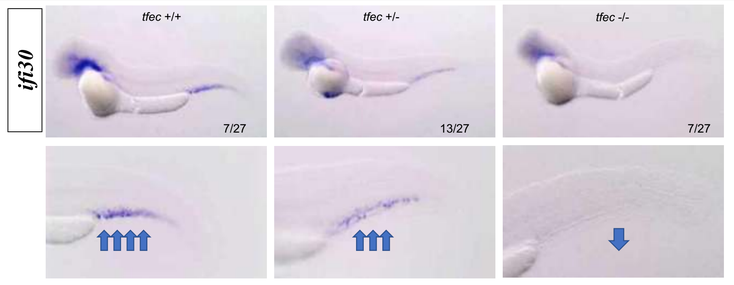
Mahony et al., Blood 2016

tfec target genes



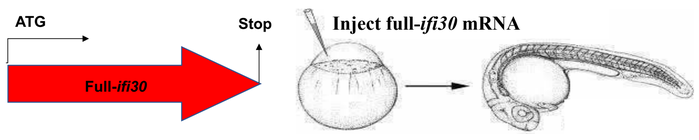
RNA Seq-Analysis

Identified around 30 genes of interest, which are up-regulated in endothelial cells



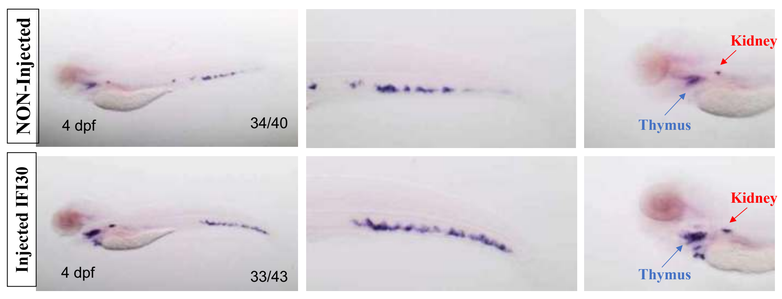
***tfec* regulates the expression of *ifi30* in the CHT at 48 hpf**

Gain of function

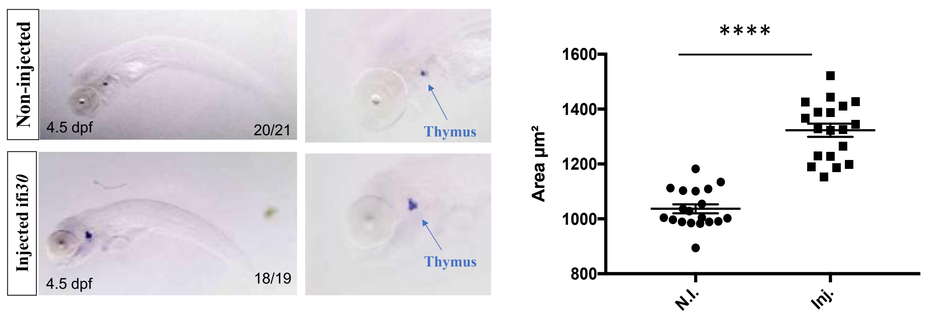


These embryos fixed at 4 and 4.5 dpf to study by WISH.

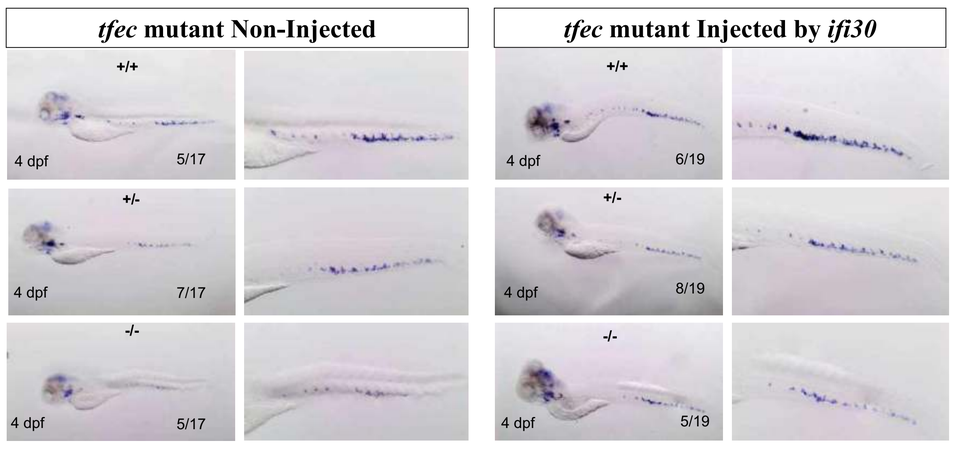
ifi30* overexpression expands the hematopoietic stem cell marker *cmyb



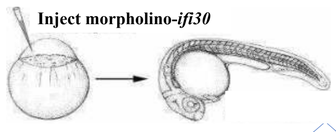
ifi30* overexpression increases the thymocytes marker *rag1



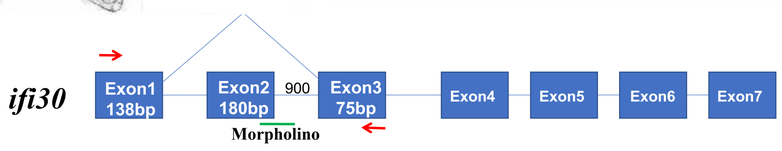
***ifi30* overexpression increases *cmyb* in *tfec* mutant**

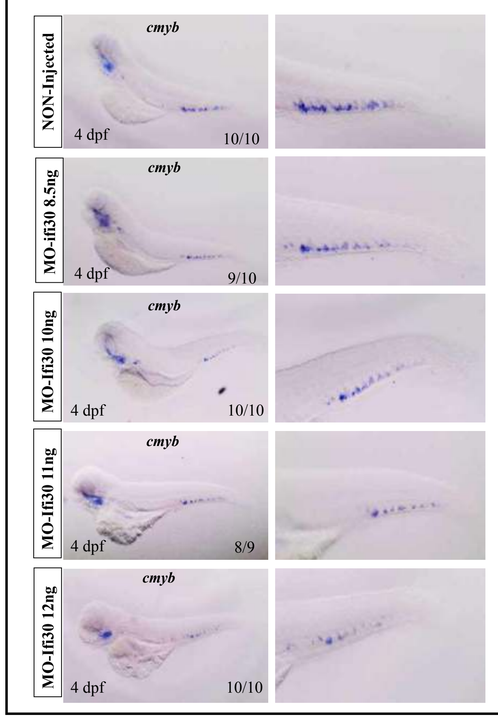


ifi30 knock-down via morpholino-modified oligonucleotide

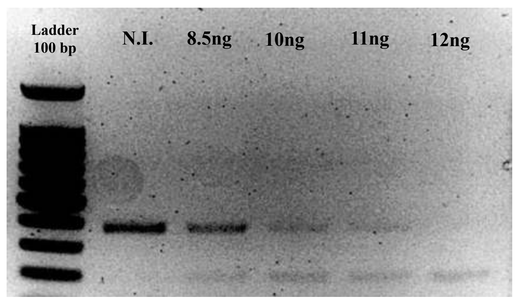


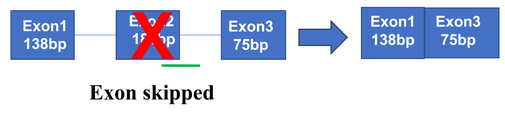
These embryos fixed at 4 dpf to study by WISH the expression of *cmyb*, an HSC marker.





Wild type = 381 bp
Morphant = 201 bp





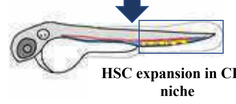
Exon skipped

PERSPECTIVE

Transcription factor *tfec*

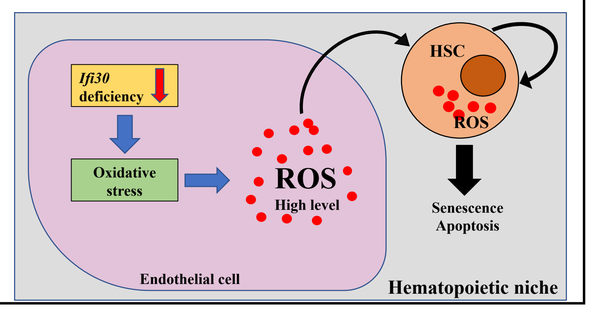
REGULATES

ifi30



HSC expansion in CHT niche

ifi30 ? **HSC**



P 5 Brain derived neurotrophic factor (BDNF) expression is associated with neural repair of injured adult zebrafish telencephalon

Pietro Cacialli [1,2,3], Livia D'angelo [2], Paolo de Girolamo [2], Luciana Castaldo [2], Olvier Kah [3], Pascal Coumailleau [3], Elisabeth Pellegrini [3], Carla Lucini [2].

[1] Department of Pathology and Immunology, CMU, University of Geneva.
[2] Dpt. Veterinary Medicine and animal production, University of Naples Federico II, Italy
[3] Inserm, UMR 1085, Research Institute in Health, Environment and Occupation, SFR Biosit, University of Rennes 1, Rennes, France

Brain derived neurotrophic factor (BDNF) belongs to the neurotrophin family, that includes nerve growth factor (NGF) and neurotrophin (NT) 3, NT 4/5 and NT 6/7. All neurotrophins interact with two types of receptors: tropomyosin-related receptor kinase (Trk) and p75 neurotrophin receptor (p75NTR). In the brain of mammals, BDNF acts through TrkB to promote neuronal survival, growth, differentiation and synaptic plasticity. In addition, BDNF has been shown to modulate, through p75NTR receptor, neuronal migration, myelination and neuronal apoptosis. Multiple promoters can modulate the tissue specific transcription of the bdnf gene. This gene is well conserved across vertebrate evolution and some regulatory sequences in the 5' UTR of the bdnf gene appear highly conserved between zebrafish and mammals, suggesting conserved functions. BDNF seems to be involved in many brain functions and plays important roles in brain plasticity and repair induced by traumatic brain lesions.

The reparative ability of the central nervous system varies widely in the animal kingdom. In the mammalian brain, the regenerative mechanisms are very limited and newly formed neurons do not survive for long time, probably due to a non-suitable local environment. By contrast zebrafish can repair their brain after injury, with fast and complete recovery of damaged area. To evaluate the potential role of BDNF in neuro-regeneration, bdnf expression was examined in the telencephalon following mechanical-lesion on adult zebrafish. bdnf mRNA levels, assessed by quantitative PCR and in situ hybridization at 1, 4, 7 and 15 days after the lesion (dpl), were increased in the damaged telencephalon, shortly after the lesion. Double staining combining in situ hybridization and immunohistochemistry revealed that bdnf mRNA expression was restricted to cells identified as early differentiated and mature neurons. Bdnf expressing neurons mostly increased in the area around the lesion, showing a peak at 1 dpl. These results highlight the role of BDNF in brain repair processes and reinforce the value of zebrafish for the study of neuro-regenerative processes.

BRAIN DERIVED NEUROTROPHIC FACTOR (BDNF) EXPRESSION IS ASSOCIATED WITH NEURAL REPAIR OF INJURED ADULT ZEBRAFISH TELENCEPHALON

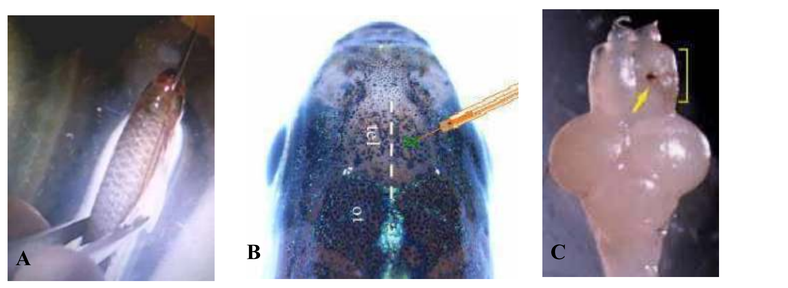
Pietro Cacialli [1,2,3], Livia D'angelo [2], Paolo de Girolamo [2],, Luciana Castaldo [2] , Marie-Madeleine Gueguen [3], Olivier Kah [3], Pascal Coumailleau [3], Elisabeth Pellegrini [3], Carla Lucini [2]

[1] Department of Pathology and Immunology, University of Geneva, Switzerland.
[2] Dpt. Veterinary Medicine and animal production, University of Naples Federico II, Italy. [3] Inserm, UMR 1085,University of Rennes 1, France
pietro.cacialli@unige.ch

ABSTRACT

Brain derived neurotrophic factor (BDNF) belongs to the neurotrophin family, that includes nerve growth factor (NGF) and neurotrophin (NT) 3, NT 4/5 and NT 6/7. All neurotrophins interact with two types of receptors: tropomyosin-related receptor kinase (Trk) and p75 neurotrophin receptor (p75NTR). In the brain of mammals, BDNF acts through TrkB to promote neuronal survival, growth, differentiation and synaptic plasticity. In addition, BDNF has been shown to modulate, through p75NTR receptor, neuronal migration, myelination and neuronal apoptosis. Multiple promoters can modulate the tissue specific transcription of the bdnf gene. This gene is well conserved across vertebrate evolution and some regulatory sequences in the 5' UTR of the bdnf gene appear highly conserved between zebrafish and mammals, suggesting conserved functions. BDNF seems to be involved in many brain functions and plays important roles in brain plasticity and repair induced by traumatic brain lesions. The reparative ability of the central nervous system varies widely in the animal kingdom. In the mammalian brain, the regenerative mechanisms are very limited and newly formed neurons do not survive for long time, probably due to a non-suitable local environment. By contrast zebrafish can repair their brain after injury, with fast and complete recovery of damaged area. To evaluate the potential role of BDNF in neuro-regeneration, bdnf expression was examined in the telencephalon following mechanical-lesion on adult zebrafish. bdnf mRNA levels, assessed by quantitative PCR and in situ hybridization at 1, 4, 7 and 15 days after the lesion (dpl), were increased in the damaged telencephalon, shortly after the lesion. Double staining combining in situ hybridization and immunohistochemistry revealed that bdnf mRNA expression was restricted to cells identified as early differentiated and mature neurons. Bdnf expressing neurons mostly increased in the area around the lesion, showing a peak at 1 dpl. These results highlight the role of BDNF in brain repair processes and reinforce the value of zebrafish for the study of neuro-regenerative processes.

TELENCEPHALON MECHANICAL INJURY



- **Zebrafish were anesthetized with tricaine methanesulfonate (MS-222).**
- **A sterile needle (BD Microlance; 0.3 mm × 13 mm) was inserted in the right side of the telencephalon, guided by landmarks on the head, following a dorso-ventral axis (Fig. 1 A-B-C).**
- **After positioning the needle tip on the surface of the skull, the pressure was applied vertically to achieve a penetration depth of 1.5 mm in the dorsal area.**

Quantitative Real-Time PCR

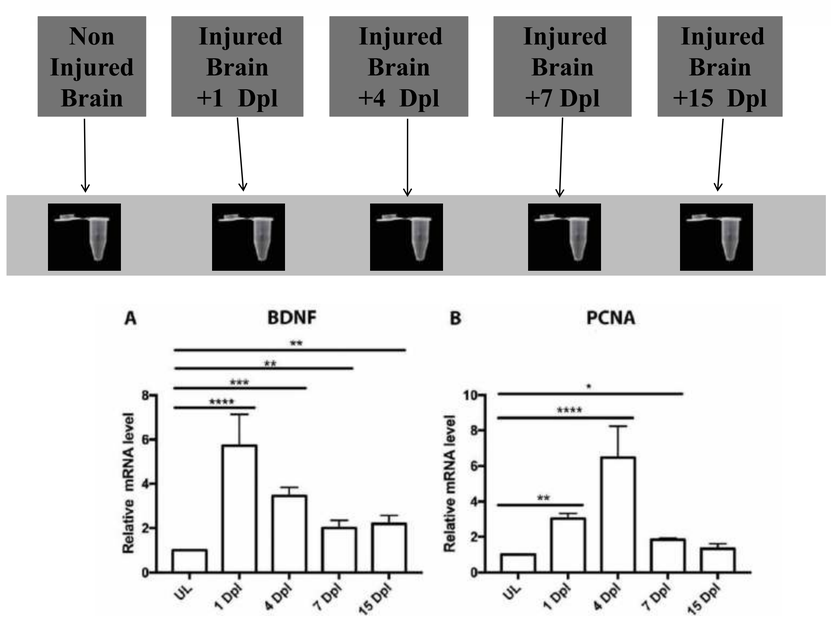


Fig. 2 BDNF (A) and PCNA (B) mRNA levels in unlesioned (UL) and injured telencephali at different point times after the lesion (1, 4, 7, 15 dpl). The asterisks indicate statistically significant differences. p<0.05 was considered statistically significant (*p<0.05; **p<0.005; p<0.001 ****p <0.0001 by t-test)

In situ hybridization

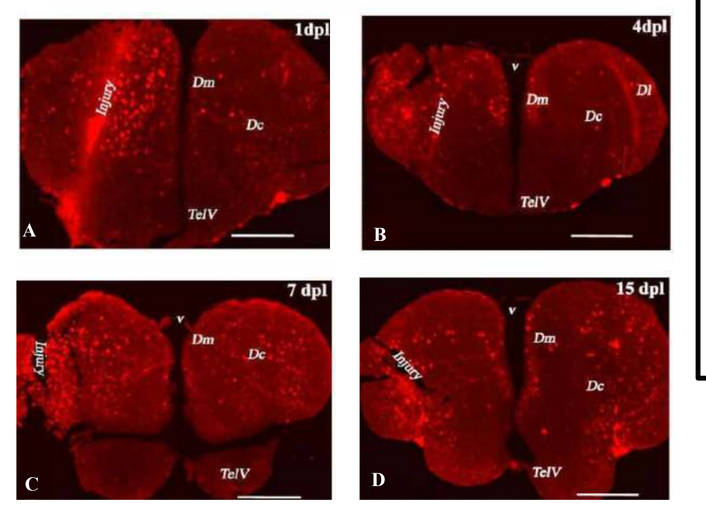
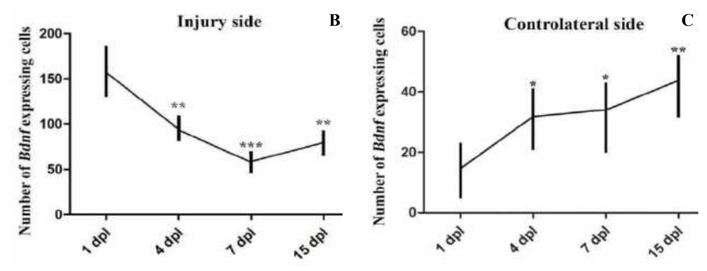
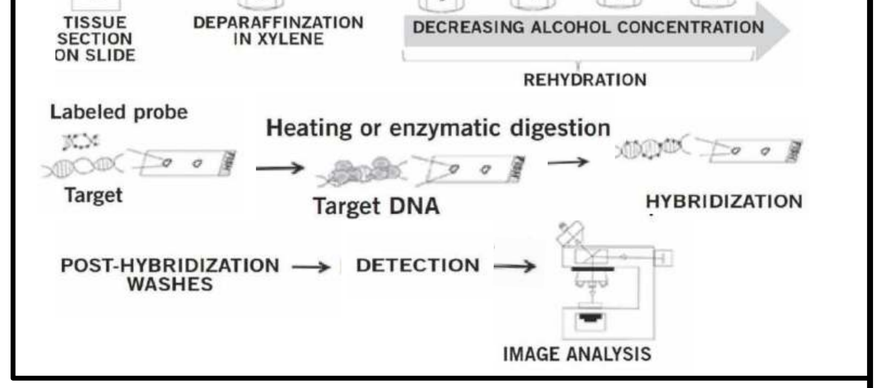


Fig. 3 BDNF mRNA expression on transversal sections of injured (left side) and non-injured telencephali (right side) at 1 dpl (A), 4 dpl (B), 7 dpl (C), 15 dpl (D). Dm: medial zone of the dorsal telencephalon; Dc: central zone of the dorsal telencephalon; Dl: lateral zone of the dorsal telencephalon; Telv: ventral telencephalon; v: ventricle.





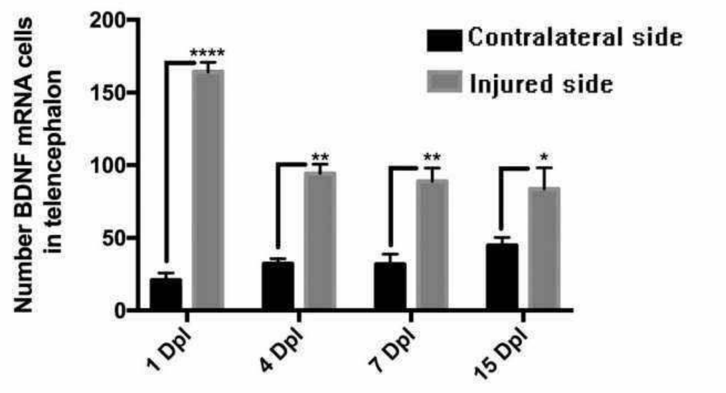


Fig. 4 Statistical analysis of the images. (A-B-C) number of BDNF mRNA cells in 5 sections (n=5) of injured and controlateral side of telencephalon at 1, 4, 7 and 15 dpl,. The asterisks indicate statistically significant difference between the values obtained in injured and controlateral side at each interval time (*p < 0.05; **p < 0.01; ***p < 0.005 using Student's t test).

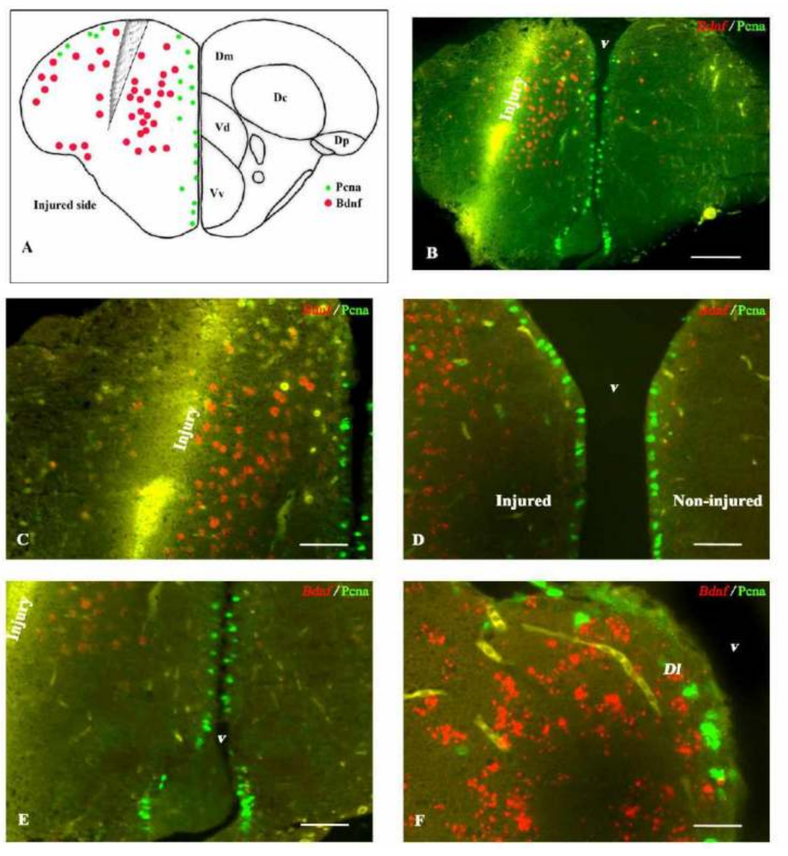


Fig. 5 Double ISH/IHC staining in injured (left side) telencephalon at 1 dpl showing BDNF mRNA (red) and PCNA protein (green). (A) is a representative section of the injured telencephalon schematically showing cells containing BDNF mRNA (red dots) and PCNA (green dots). At low (B), middle (C, D, E) and high (F) magnification.

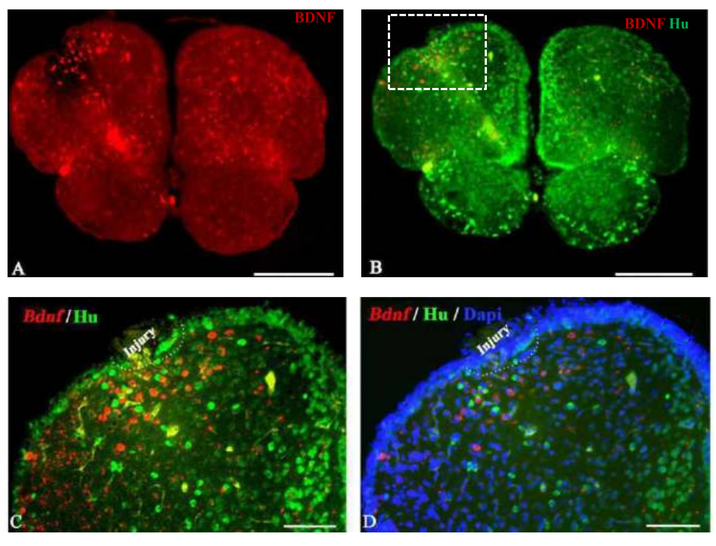


Fig. 6 Double ISH/IHC staining in injured (left side) telencephalon of 1 dpl zebrafish showing BDNF mRNA (red) and Hu/c protein, early neural marker (green). C, D are high magnification of the rectangular areas showed in B. In D cell nuclei are counterstained in blue with DAPI.

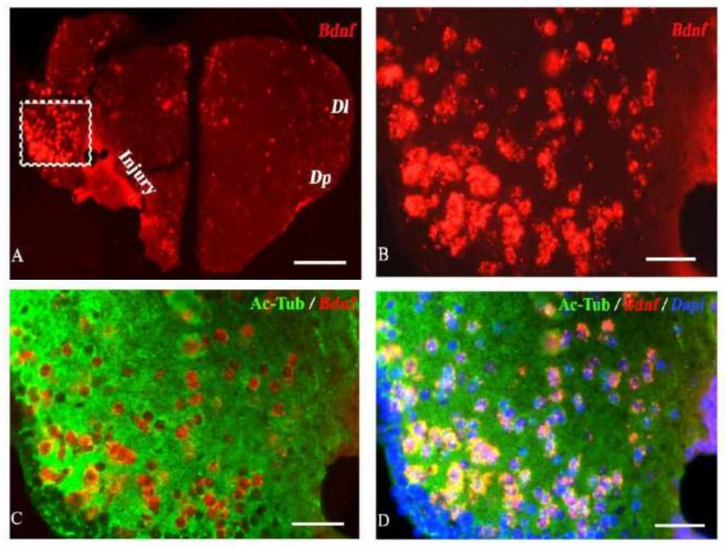


Fig. 7 Double ISH/IHC staining in injured (left side) telencephalon of 1 dpl zebrafish showing BDNF mRNA (red) and acetylated-tubulin, mature neuron marker (green). B, C, D are magnification of the rectangular area showed in A. In D cell nuclei are labeled in blue with DAPI.

CONCLUSION

These results show for the first time, the involvement of BDNF during regenerative processes in the adult fish brain after injury. In zebrafish BDNF mRNA presence persists around the lesioned area. Considering the complete repair of the damaged area in fish, it is possible that BDNF is a factor contributing to creating a permissive environment that enables the establishment of new neuronal populations in damaged brain.

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ZDM12

The endothelial niche detoxifies HSCs from ROS in the caudal hematopoietic tissue.

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Presenter: **Pietro Cacialli**

Hematopoietic stem cells (HSCs) are responsible for sustaining hematopoietic homeostasis. In the adult, it has been well established that their functions can be affected by reactive oxygen species (ROS) that are produced endogenously through cellular metabolism or after exposure to exogenous stress. An increase of ROS can inhibit HSC self-renewal and induce HSC senescence, resulting in premature exhaustion of HSCs and hematopoietic dysfunctions. Here we show that ROS similarly affect HSCs during their expansion phase in the embryo. We show that connexins are important in regulating ROS levels in HSCs. Indeed, their inhibition increases the level of ROS in HSCs and induces their cell-death in the Caudal Hematopoietic Tissue (CHT) niche of zebrafish embryos. The loss of HSCs after connexin inhibition can be rescued by reduced-Glutathione (GSH) treatment. In cells, GSH levels can be modulated by several enzymes. Here, we show the importance of a new gene in this process: Gamma-interferon-inducible lysosomal thiol reductase (GILT/ifi30), an important enzyme for antigen presentation in the context of immunity, can rescue the HSC loss resulting from ROS toxicity. Unexpectedly, we found that ifi30 was highly expressed in endothelial cells (ECs) from the CHT, but not in HSCs. Endothelial-specific ifi30 overexpression increased HSCs expansion in the CHT. Moreover, we found a high increase of ROS in ifi30-deficient embryos, resulting in a defect of HSC expansion in the CHT. This defect was rescued by several anti-oxidants: GSH and N-acetyl-cysteine. Altogether, our data show that HSCs transfer ROS to the endothelial niche, where all the tools are expressed to detoxify the microenvironment. This new role of ifi30 seems to be conserved during human embryogenesis as most of immature hematopoietic progenitors are associated with IFI30/GILT expressing cells in the human fetal liver.

ZDM14 Abstract Booklet Directory

ZDM14 Abstract Directory - By Last Name

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Burton	Edward	O-002	Drug discovery and chemical biology	Unbiased chemical screen in a novel zebrafish model identifies a molecular modulator of neuroinflammation in tauopathy
Burton	Alexander	P-085	Drug discovery and chemical biology	Sinusoidal analysis reveals a non-linear and dopamine-dependent relationship between ambient illumination and motor activity in larval zebrafish
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Zhu	Yunlu	O-038	Neurological and behavioral disease	Linking molecular abnormalities to behavioral deficits using a zebrafish model for tauopathies

VIRTUAL 11th EUROPEAN ZEBRAFISH MEETING 2020

October 26 - 27, 2020

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Certificate of Attendance

Zebrafish 2020 Virtual Meeting organisers certify that

Pietro Cacialli

attended Zebrafish 2020 Virtual Meeting held online on 26th and 27th October 2020.

Petr Bartunek

Local Organizing Committee Chair

CERTIFICATE OF ATTENDANCE

THIS CERTIFIES THAT

Pietro Cacialli

has attended the 12th Zebrafish Disease Models Conference

July 15-18, 2019

At The Joseph B. Martin Conference Center
At Harvard Medical Center
In Boston, Massachusetts

ZDMS

ZDM12
Boston | USA 2019

ZDM12 CONFERENCE AWARD

PRESENTED TO:

Pietro Cacialli

ON

Thursday, July 18, 2019

Second PANACHE meeting

Monday November 22, 2021:
on-line meeting, free of charge

8.50h: **Welcome** (Brenda Kwak / Mathieu Vinken)

Session 1: Points of attention in biomedical research
Chair: Brenda Kwak (UNIGE, Switzerland)

9h: **Circadian rhythm in inflammation** – Christoph Scheiermann (University of Geneva, Switzerland)

9.30h: **Sex differences in atherosclerotic mechanisms** – Hester den Ruijter (University Medical Center Utrecht, the Netherlands)

10h: **The influence of the gut microbiome on the course of inflammatory disease** – Simone Becattini (University of Geneva, Switzerland)

10h30: **Blood flow and vascular inflammation** – Paul C. Evans (University of Sheffield, UK)

11h-11h20: General discussion and wrap-up

COFFEE BREAK (11h20-11h35)

Session 2: Connexins in health and disease
Chair: Maria Mayan (INIBIC, Spain)

11.35h: **Keynote Lecture 1**

Arantxa Tabernero (University of Salamanca, Spain) -
Therapeutic applications of Src inhibitory peptides based on connexin43

12.20h-13h: **Flash presentations** (7 min presentation, 3 min discussion)

Axelle Cooreman (VUB, Belgium) -
Effect of COVID-19 drugs on connexin43

Harry Scott (University of Glasgow, UK) -
The human Discs large protein (Dlg1) controls Connexin 43 (Cx43) trafficking to the plasma membrane and gap junctional communication in keratinocytes

Jade Montgomery (University of Geneva, Switzerland) -
Ain't nothing but a heartbreak: Effects of chronic hypoxia on cardiac ischemic injury response

Marc Mesnil (University of Poitiers, France) -
Implication of connexin43 in glioma invasion

LUNCH BREAK (13h-14h15)

Session 3: Connexins/pannexins in health and disease

Chair: Steven Ballet (VUB, Belgium)

14h15-16h: **Flash presentations** (7 min presentation, 3 min discussion)

Alejandro Garcia-Yuste (INIBIC, Spain) -
Role of connexins in intervertebral disc degeneration

Kaat Leroy (VUB, Belgium) -
Connexin-based channel activity is not specifically altered by hepatocarcinogenic chemicals

Andrea Álvarez Vázquez (University of Salamanca, Spain) -
Effect of the Src inhibitory peptide TAT-Cx43$_{266-283}$ in neural stem cells with EGFR overexpression or EGFRvIII mutation

Theresa Rodrigues (University of Coimbra, Portugal) -
USP8 modulates Cx43 homeostasis in endothelial cells

Pietro Cacialli (University of Geneva, Switzerland) -
A connexin/ifi30 pathway bridges HSCs with their niche to dampen oxidative stress

Laureano Carpio (ProtoQSAR SL, Spain) -
AlphaFold: a revolution in biology and medicine. Examples in the case of Connexins and Pannexins

COFFEE BREAK (15h15-15h30)

Paula Carpintero-Fernandez (INIBIC, Spain) -
Targeting drug resistance in breast cancer

Malaury Tournier (University of Geneva, Switzerland) -
Studying Pannexin1 channel function in cardiovascular diseases

Anne Caufriez (VUB, Belgium) -
Effects of drugs for the treatment of COVID-19 on pannexin1 channels

16h-16.45h: **Keynote Lecture 2**

Brant Isakson (University of Virginia School of Medicine, USA) -
Dunning-Kruger experiences with pannexins in the vasculature

Grant agreement number 858014

A connexin/ifi30 pathway bridges HSCs with their niche to dampen oxidative stress.

Pietro Cacialli [1], Julien Y. Bertrand [1]
[1] Department of Pathology and Immunology, School of Medicine, University of Geneva, Switzerland.

Presenter: **Pietro Cacialli**

Abstract

Reactive oxygen species (ROS) represent a by-product of metabolism and their excess is toxic for hematopoietic stem and progenitor cells (HSPCs). During embryogenesis, a small number of HSPCs are produced from the hemogenic endothelium, before they colonize a transient organ where they expand, for example the fetal liver in mammals. In this study, we use zebrafish to understand the molecular mechanisms that are important in the caudal hematopoietic tissue (equivalent to the mammalian fetal liver) to promote HSPC expansion. High levels of ROS are deleterious for HSPCs in this niche, however this is rescued by addition of antioxidants. We show that Cx41.8 is important to lower ROS levels in HSPCs. We also demonstrate a new role for ifi30, known to be involved in the immune response. In the hematopoietic niche, Ifi30 can recycle oxidized glutathione to allow HSPCs to dampen their levels of ROS, a role that could be conserved in human fetal liver.

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PhD School of Life Sciences, University of Geneva, Faculty of Medicine
1, rue Michel Servet | 1206 Geneva | Switzerland
http://lifesciencesphd.unige.ch/

Geneva, 04.11.21

Concern: Certificate

Pietro CACIALLI has been acting as tutor for the module Cell interaction he did:

6 teaching hours total in October 2021

Pietro Cacialli did a total of 6 teaching hours for the doctoral school.

With best regards,

Prof. Dominique GARCIN
Program director, Biomedical Sciences,
Faculty of Medicine
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To whom it concerns

I have known Pietro Cacialli since he started working as PhD student in April of 2013 in my laboratory at the Department of Veterinary Medicine of University of Naples Federico II in Italy. He integrated perfectly within my group and has contributed significantly to move his project forward. In detail, he studied the presence and localization of neurotrophins in the brain of larva and adult zebrafish, using basic histological methods, immunohistochemistry, in situ hybridization (ISH), western blotting and qPCR analysis. He achieved excellent expertise at confocal microscopy.

During his training period, he also decided to extend his studies on neural stem cell and brain regeneration. He spent one year at the laboratory of neurobiology of IRSET that was directed by Prof. Olivier Kah at University of Rennes, in France. Pietro also obtained an award for his research on BDNF. In this period, Pietro learnt to master a difficult technique to induce an injury in adult zebrafish brain. He used this technique to study the role of BDNF during the regenerative event after traumatic brain injury in adult zebrafish.

The results he achieved during his PhD studies were published and reviewed in 7 papers:
Cacialli P. et al., Plos One 2016; **Cacialli P.** et al., J. Comp. Neurology 2018; **Cacialli P.** et al., Anatomical record 2018; **Cacialli P.** et al., Neural Reg. Res. 2018; Lucini et al., Int. J. Mol. Scie. 2018; **Cacialli P.** et al., J. Anatomy 2019; **Cacialli** and Lucini Neural Reg. Res. 2019.

As assistant, Pietro has carried out several hours (60 hours) of supplementary teaching in animal anatomy, cytology and histology for students of the degree course in veterinary medicine at Department of Veterinary Medicine at the University of Naples Federico II.

In summary, already at the beginning of his scientific carrier, Pietro Cacialli demonstrated real excellent capacities, strong dynamism and indefatigable enthusiasm.

Naples, 20 January 2022,

In witness there of Prof. Carla Lucini

UNIVERSITÉ DE GENÈVE
FACULTÉ DE MÉDECINE

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Dear members of the Committee,

It is my pleasure to enthusiastically support the application of Dr. Pietro Cacialli, Ph.D. to a*n Assistant Professor position*. Pietro is a talented scientist, he started in my laboratory in December 2016. Recently he obtained a promotion as "Maitre Assistant" (start on October 2021) that allowed to stay in my laboratory for next three years, if necessary, as he is actively looking for independent PI positions. Of note, Pietro as independent young investigator has already applied to grants for diseases affecting children and this project was awarded CHF-50'000 (November 2020) from the Gertrude von Meissner Foundation, and CHF-30'000 (May 2021) from the Ernest Boninchi Foundation.

Before he joined me, Pietro performed his PhD thesis at the University of Naples "Federico II" (Naples, Italy) and University of Rennes1 (Rennes, France). There, he identified the role of neurotrophins within the neural stem cell niche, during the regenerative process that occurs after traumatic brain injury in the zebrafish model. This work has allowed him to publish several papers, and acquainted him with the zebrafish model and the neurobiology field and techniques, which he will further develop in his future group.

In my laboratory, Pietro has been interested to extend his studies of the Stem Cell niche to another, better characterized system in the zebrafish: the hematopoietic stem cell (HSC) niche. Indeed, in my laboratory, we are trying to characterize the role of new genes that regulate the specification, expansion and differentiation of HSCs during zebrafish embryonic development. Pietro showed a strong interest in the genetic regulation of HSC expansion at the non-cell-autonomous level, and how these can be utilised to improve current regenerative medicine therapies. He is currently working on several new genes that seem to be really important for HSCs as their knockouts result in loss of HSCs at different stages. All these genes have in common that they are all controlled by *tfec*, a transcription factor of the MITF family. His first paper has been published in **Nature Communications** 2021. This manuscript addresses the molecular pathways that are involved in the control of oxidative stress underwent by HSC, by their microenvironment. Pietro has also submitted another manuscript where he has identified all the cellular and molecular pathways involved in the stimulation of HSCs by prostaglandin E2, a key regulator of HSC expansion during embryonic life. This paper has also been reviewed by **EMBO**, and we are now successfully addressing reviewers' comments. Finally, Pietro has contributed to another paper, published in **Blood Advances.**

At the same, during these years as Postdoc and actually as Maitre assistant (he is teaching in different modules for student of PhD School of Life Sciences and Faculty of Medicine), he also supported me to train and supervise several PhD and master students' in biomedical science at our laboratory. In detail he supervised:
Mr. Serkan Dogan (Master's student), Title of thesis: *Mcm10 regulates the emergences of HSCs from the dorsal aorta of zebrafish embryo*, (2021);

Mr. Julien Angiolillo (Master's student), Title of thesis: *Cndp2 is involved in expansion of HSCs in the CHT of zebrafish embryo*, (2020);
Mrs.Tanya Linnertz (PhD obtained on 2018); Title of thesis: *Identifying new regulators of cardiovascular development*
Mr. Joey J. Ghersi (PhD obtained on 2018); Title of thesis: *Bif1, a new BMP signaling inhibitor, regulates embryonic hematopoiesis in the zebrafish*
Etienne Gomez (ongoing);
Tim Petzold (ongoing).

In parallel to this work, Pietro has initiated his own, independent line of research, which he would like to develop in his future laboratory.

Pietro has reconnected with his PhD work on the neural stem cell niche, by re-using all the knowledge and the tools he has developed in the context of the hematopoietic niche. Indeed, by examining the mutants (*tfec* target genes, such as *cathepsin-B* and *L*), he found out that these embryos harboured a strong neural phenotype as they showed a huge decrease in neurogenesis. Pietro linked this phenotype to a lysosomal storage disease, and as I mentioned before, his project was awarded by two different foundations.

Altogether, Pietro Cacialli is on his way to independence, as he started new lines of research that are completely different from our scientific goals in my laboratory. As the path to a group leader position is long, it is important to support him in his career development and I hope you will positively consider him for additional support,

Best regards,

Dr. Julien Bertrand, Ph.D.
Associate Professor.

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February 17, 2022

Reference letter for Pietro Cacialli, PhD

Dear members of the selection committee,

I support the application of Dr. Pietro Cacialli for an Assistant professorship.

Dr. Cacialli has joined as a Postdoc and actually Maitre assistant the laboratory of Prof. Julien Bertrand in the Department of Pathology and Immunology at the University of Geneva, Switzerland. Dr. Cacialli rapidly integrated in the Department by participating actively in common activities.

Dr. Cacialli is an active member of our Department, indeed he is involved in organizing our seminars, progress reports and departmental retreats.

As department director but also as an established connexin researcher, I particularly enjoyed his exciting and didactic presentations at our progress reports.

Using zebrafish as a model system, Dr. Cacialli studies hematopoiesis, and more particularly the cell and non-cell autonomous signals that drive hematopoietic stem cell specification, expansion and differentiation. As may be inferred from his recent publication in Nature Communications (2021), he has successfully investigated and described the mechanisms that control inflammation in the hematopoietic niche to preserve blood stem cells.

I remain at your disposal for further information.

Sincerely yours,

Prof. Brenda R. Kwak, PhD