DOCTORAT ECOLOGIE
BRETAGNE GEOSCIENCES
LOIRE AGRONOMIE ALIMENTATION

PhD PROPOSAL FOR THE DOCTORAL SCHOOL

« Ecologie, Géosciences, Agronomie, ALimentation »

GENERAL INFORMATION

Thesis title: **Impact of adipose tissue development on myogenesis in trout**
Acronym: MyoAd
Disciplinary field 1: Agronomy **Disciplinary field 2:** Food science
Three keywords: muscle; adipocyte; stem cells
Research unit : UR1037 Fish Physiology and Genomics Laboratory
Name of the thesis director HDR (Habilitation thesis to supervise research) required: **Jean-Charles Gabillard** **Email address of the thesis director: jean-charles.gabillard@inrae.fr** **Name of the thesis co-director (if applicable): HDR (Habilitation thesis to supervise research) required:** **Email address of the thesis co-director (if applicable):** **Name of the thesis co-supervisor 1 (if applicable): Isabelle Hue** **Email address of the thesis co-supervisor 1 (if applicable): isabelle.hue@inrae.fr** **Name of the thesis co-supervisor 2 (if applicable):** **Email address of the thesis co-supervisor 2 (if applicable):**
Thesis grant (funding origin and amount): 50%INRAE 50 % Région Bretagne ; 1875€
Contact(s) (mailing address and E-mail): INRAE – LPGP Campus de Beaulieu 35000 Rennes
Recruitment process: Recruitment process depends on thesis funding. To select the corresponding recruitment process, please visit the EGAAL website here. This information is needed for proposal publication. ☐ Doctoral school contest X Interview ☐ Other (indicate) :

All sections must be filled. Once filled, please save the proposal form in pdf format using the following naming: Supervisor Name_Unit_Subject Acronym_EN.pdf

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SCIENTIFIC DESCRIPTION OF THE PhD PROJECT

Socio-economic and scientific context : (10 lines)

Skeletal muscle, made of muscle, fat and connective tissues (TM, TA, TC), determines most of the quality of the meat through its growth, organisation and composition. However, the interactions (molecular, cellular) between these tissues during their growth are poorly understood.

In certain human pathologies or agronomic species, it has been shown that the modification of one of these tissues can impact the development of the others. In double-muscled cattle, the strong development of muscle tissue is accompanied by a reduction in intramuscular fat tissue (Bonnet et al 2010). Conversely, some cases of obesity in humans are accompanied by muscle wasting (Lipina et al 2017). In vitro, in humans and mice, "myotube/adipocyte" co-cultures from obese subjects showed that visceral adipocytes were more capable, through their secretome (cytokines in particular), of disturbing muscle cells than subcutaneous adipocytes were. In response, the muscle would produce altered amounts of myokines affecting the endocrine function of visceral adipose tissue (Pellegrini, 2015, Bonnet et al 2020). Thus, in mammals, interactions between adipose and muscle tissue development exist and are finely tuned.

In trout, preliminary data obtained in selected lines diverging in subcutaneous and intramuscular adipose tissue content (fat vs. lean, 7th generation) show a higher fibre number (+65%) in the lean line at the portion stage (300g) (Lefèvre et al 2015, 2016, unpublished data). However, to date no data are available on the interactions between adipose tissue and muscle tissue in trout.

Assumptions and questions (8 lines)

Our working hypothesis is that high adipose tissue development would influence the size and number of fibres and the myogenic capacity of muscle stem cells by modifying the interactions between adipocytes and muscle stem cells (satellite cells). The proposed research program aims to determine the impact of high adipose tissue development on myogenesis (hyperplasia and hypertrophy) in trout.

The main steps of the thesis and scientific procedure (10-12 lines)

1) Characterization of post-larval development of fat and muscle tissue in fat and lean lines

Since our team has shown that the trout (300g) of the lean line had fibres with a smaller average diameter (Lefèvre et al 2015), we will determine at what stage this difference appears and if this kinetic is associated with the development of the adipose tissue. To do this, we will quantify adipose tissue (subcutaneous and intramuscular) and muscle tissue (size and number of fibres) in trout from 5g (presence of detectable adipose tissue) to 300g (difference in muscle fibre size). This histological quantification of adipose tissue will be done using the lipidTox. In addition, for each stage, we will also measure by in situ hybridization (RNAscope), the adipogenic (perilipin, Dlk1, ...) and myogenic (Pax7, Myomaker) activity.

2) Characterization of the myogenic capacities of satellite cells of fat and lean trout lines.

To determine whether the myogenic potential of satellite cells is different in the two trout lines, we will extract these cells from the white muscle of 5g and 100g trout (to be redefined according to the results of axis 1). We will analyze their proliferation capacity by quantifying the rate of cells that have incorporated BrdU for 24 hours, and their differentiation by immunocytofluorescence (myogenin and myosin) (Gabillard et al 2010).

3) Characterization of cellular interactions between adipocytes and satellite cells

The aim is to determine, using co-culture, to what extent adipocytes from fat and lean fish lines can modify the proliferation and/or differentiation of satellite cells. 24 hours after seeding the satellite cells, the adipocytes will be added and the co-culture will be continued for 72 hours in DMEM medium with serum at 18°C. Furthermore, we will be able to determine whether intramuscular, subcutaneous and perivisceral adipocytes have the same impact on satellite cells.

Methodological and technical approaches considered (4-6 lines)

The candidate will develop cell culture (primary culture, co-culture), histology (immunocytofluorescence, 3D

analysis) and molecular biology (qPCR, RNAscope) approaches. The candidate will also be required to carry out all the statistical analyses necessary for the analysis of the results.
Scientific and technical skills required by the candidate The candidate should have solid knowledge and experiences in cell and tissue biology. In addition, the candidate should have a basic knowledge of cell culture and statistics (R software).

THESIS SUPERVISION[1]

Unit name: Fish Physiology and Genomics laboratory	**Team name:** Growth and flesh quality
Unit director name: Julien Bobe	**Team director name:** Jean-Charles Gabillard
Mailing address of the unit director: Julien Bobe	**Mailing address of the team director:** Jean-Charles Gabillard
Thesis director Surname, first name: Jean-Charles Gabillard Position: Research director Obtained date of the HDR (Habilitation thesis to supervise research): 2014 Employer: INRAE Doctoral school affiliation: EGAAL Rate of thesis supervision in the present project (%): 50% Total rate of thesis supervision in ongoing theses (supervisions and co-supervisions) (%): 0% Number of current thesis supervisions/co-supervisions: 0	
Thesis co-director Surname, first name: Position: Obtained date of the HDR (Habilitation thesis to supervise research): Employer: Doctoral school affiliation: Rate of thesis supervision in the present project (%): Total rate of thesis supervision in ongoing theses (supervisions and co-supervisions) (%):	

1 **In EGAAL Doctoral School, if only one scientist in thesis supervision = 100% of supervision rate; if 2 people involved in thesis supervision = from 50% to 70% of supervision rate for the director; if 3 people involved in thesis supervision = 40% / 30% / 30% of supervision rate distribution among supervisors.**

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Number of current thesis supervisions/co-supervisions:

Thesis co-supervisor 1 (if applicable)

Surname, first name: Isabelle Hue

Position: Research scientist

Habilitation thesis to supervise research ☐ yes X no If yes, date diploma received:

Employer: INRAE

Doctoral school affiliation: EGAAL

Rate of thesis supervision in the present project (%): 50%

Total rate of thesis supervision in ongoing theses (supervisions and co-supervisions) (%):0%

Number of current thesis supervisions/co-supervisions: 0

Thesis co-supervisor 2 (if applicable)

Surname, first name:

Position:

Habilitation thesis to supervise research ☐ yes ☐ no If yes, date diploma received:

Employer:

Doctoral school affiliation:

Rate of thesis supervision in the present project (%):

Total rate of thesis supervision in ongoing theses (supervisions and co-supervisions) (%):

Number of current thesis supervisions/co-supervisions:

Private partner (if CIFRE funding, private funding,…)

Surname, first name:

Position:

Employer:

Rate of thesis supervision in the present project (%):

Total rate of thesis supervision in ongoing theses (supervisions and co-supervisions) (%):

Number of current thesis supervisions/co-supervisions:

International partner (if Cotutelle thesis)

Surname, first name:

Position:

Employer:

Rate of thesis supervision in the present project (%):

Total rate of thesis supervision in ongoing theses (supervisions and co-supervisions) (%):

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Number of current thesis supervisions/co-supervisions:

Professional status of previous PhD students supervised by both director and co-supervisors (from 5 years)

Please provide the following information for each PhD students supervised

Surname, first name: Aurélie Landemaine

Date of PhD beginning and PhD defence: 1/11/2012 - 31/10/2015

Thesis supervision: Pierre-Yves Rescan then Jean-Charles Gabillard

Professional status and location: Self-employed, Rennes

Contract profile (post-doc, fixed-term, permanent):

List of publications from the thesis work:

Landemaine, A., Ramirez-Martinez, A., Monestier, O., Sabin, N., Rescan, P.-Y., Olson, E.N., Gabillard, J.-C. 2019. Trout myomaker contains 14 minisatellites and two sequence extensions but retains fusogenic function. Journal of Biological Chemistry, 294 (16): 6364-6374. http://dx.doi.org/10.1074/jbc.RA118.006047

Monestier, O., Landemaine, A., Bugeon, J., Rescan, P.-Y., Gabillard, J.-C. 2019. Naa15 knockdown enhances c2c12 myoblast fusion and induces defects in zebrafish myotome morphogenesis. Comparative Biochemistry and Physiology. Part B, Biochemistry and Molecular Biology, 228: 61-67. http://dx.doi.org/10.1016/j.cbpb.2018.11.005

Landemaine, A.; Rescan, P.Y.; Gabillard, J.C., 2014. Myomaker mediates fusion of fast myocytes in zebrafish embryos. Biochemical and Biophysical Research Communications, 451 (4): 480-484. http://dx.doi.org/10.1016/j.bbrc.2014.07.093

Surname, first name: Sabrina Jagot

Date of PhD beginning and PhD defence: 1/11/2015 - 31/10/2018

Thesis supervision: Jean-Charles Gabillard

Professional status and location: ONIRIS, Nantes

Contract profile (post-doc, fixed-term, permanent): post-Doc

List of publications from the thesis work:

Jagot, S., Sabin, N., Le Cam, A., Bugeon, J., Rescan, P.-Y., Gabillard, J.-C. 2018. Histological, transcriptomic and in vitro analysis reveal an intrinsic activated state of myogenic precursors in hyperplasic muscle of trout. BMC Genomics, 19:865: 1-11. http://dx.doi.org/10.1186/s12864-018-5248-y

Five main recent publications of the supervisors on thesis subject:

Bou M, Montfort J, Le Cam A, Rallière C, Lebret V, Gabillard JC, Weil C, Gutierrez J, Rescan PY, Capilla E, Navarro I (2017). Gene expression profile during proliferation and differentiation of rainbow trout adipocyte precursor cells. BMC Genomics 18: 1-20 .

Jagot S, Sabin N, Le Cam A, Bugeon J, Rescan PY, Gabillard JC. (2018). Histological, transcriptomic and in vitro analysis reveal an intrinsic activated state of myogenic precursors in hyperplasic muscle of trout. BMC Genomics 19:865

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Monestier O, Landemaine A, Bugeon J, Rescan PY, Gabillard JC. (2019). Naa15 knockdown enhances c2c12 myoblast fusion and induces defects in zebrafish myotome morphogenesis. Comparative Biochemistry and Physiology, Part B 228 61–67

Landemaine A, Ramirez-Martinez A, Monestier O, Sabin N, Rescan PY, Olson EN, Gabillard JC. (2019). Trout myomaker contains 14 minisatellites and two sequence extensions but retains fusogenic function. J. Biol. Chem. 294(16) 6364 –6374

Biase F, Hue I, Dickinson S, Jaffrezic F, Laloe D, Lewin H, Sandra O., 2019. Fine-tuned adaptation of embryo-endometrium pairs at implantation revealed by transcriptome analyses in Bos taurus. PloS Biol, 17 (4): e3000046

THESIS FUNDING

Origin(s) of the thesis funding: INRAE/PHASE (50 % acquis) et Région Bretagne (50 %, pending response)
Gross monthly salary: 1875€
Thesis funding state : Acquired
Funding beginning date/Funding ending date: 1/10/2021 (36 months)

Date: 23th March 2021

Name, signature of unit director: Julien Bobe

Name, signature of team director: Jean-Charles Gabillard

Name, signature of thesis project director: Jean-Charles Gabillard