

### THESIS TOPIC

Subject N° (to be completed by the ED):	<b>FUNDING:</b> <input checked="" type="checkbox"/> Requested <input type="checkbox"/> Acquired	Funding origin:
Thesis title: <b>C-UA- Preconception maternal bariatric surgery and the consequences on cardiovascular and hepatic functions of the mother and offspring</b>		3 keywords: maternal obesity, bariatric surgery, fetal programming
Unit / team: <b>Mitovasc laboratory, Carme team (Cardiovascular Physiopathology)</b>		
Supervisor's name: <b>Dr Céline Fassot</b>	Phone number: +33 2 44 68 82 71 Email address: celine.fassot@inserm.fr	
<p><u>Socio-economic and scientific context (approximately 10 lines):</u>          Cardiovascular pathologies are the leading cause of mortality worldwide and their link with the development of obesity has been widely demonstrated. It is also well known that children born to obese mothers have a higher susceptibility to develop obesity and then cardiovascular pathologies during adulthood, through programming of tissue functions induced by <i>in utero</i> hyperglycemic environment. Bariatric surgery is the most effective treatment for morbid obesity and many women of childbearing age use it. But if these interventions improve fertility, maternal and fetal prognosis, there is very little data on their impact on the outcome of cardiovascular and hepatic alterations in operated mothers and on the prevalence of cardiovascular diseases in their children. Our preliminary preclinical data highlight differential effects depending on the type of bariatric surgery (restrictive or mix surgery) in the offspring: offspring born to female rats with sleeve gastrectomy seem to have an intermediate metabolic profile compared to those born to obese or normal-weight mothers. Gastric bypass appears to induce intrauterine growth retardation hampering the development of pups, possibly linked to abnormalities of the uterine vessels.</p> <p>Maternal bariatric surgery could thus induce constitutional modifications, through epigenetic mechanisms, intestinal microbiota, and/or vitamin and microelement deficiencies during gestation and lactation, which would lead to increased susceptibility of offspring to the occurrence of metabolic, cardiovascular, and hepatic abnormalities.</p>		
<p><u>Working hypothesis and aims (approximately 8 lines):</u>          This project is the first to focus on the two most widely used bariatric surgery (sleeve and gastric bypass) and their impact not only on mother but also on children cardiovascular and hepatic health. The aim of this thesis is to study the hepatic and cardiovascular functions of the descendants born to female rats with restrictive bariatric (sleeve gastrectomy), or restrictive and malabsorptive (gastric bypass) surgery in comparison to offspring born to normal-weight or obese mothers. The experimental results could be transposed into the clinical field, based on existing cohorts and biocollections at the Angers University Hospital. The final objective is to improve the care of operated mothers and their children, in terms of prevention, health promotion and early management of comorbidities linked to obesity. This project is thus integrated into the current public health objectives to counteract the development of obesity and associated cardiovascular diseases.</p>		
<p><u>Main milestones of the thesis (approximately 12 lines):</u>          - The first year of the thesis will be mainly dedicated to the end of the constitution of the different groups of mothers and offspring, with a particular focus on the middle-term consequences on the mothers (analysis of liver and cardiovascular functions, intestinal microbiota, arterial pressure).          - The second year will allow to study the effects of bariatric surgery on the offspring and will correspond to the analysis of the different tissues and biological samples taken from the animals during sacrifice: analyzes of the vascular reactivity of the mesenteric arteries and the aorta, histomorphometry of these vessels, evaluation of cardiac function and hepatic structure, structural analysis and inflammation of adipose tissues, search for vitamin and/or essential nutrients deficiency...          - The last part of this project will concern the study of fetal programming: (1) analysis of the microbiota to look for correlations with alterations in vascular, adipose and hepatic tissues; (2) analysis of cardiovascular epigenetic modifications.</p>		
<p><u>Scientific and technical skills required by the candidate (2 lines):</u>          - Licence for animal experimentation          - Use of standard laboratory analysis (western blot, ELISA, immunohistochemistry, PCR, etc.) and skills in vascular and/or hepatic functional analyses, microbiota</p>		
<p><u>3 publications from the team related to the topic (last 5 years):</u>          - Payen C, Guillot A, Chaigneau J, Bichot L, Gascoin G, Vessières E, Loufrani L, Schmitt F, <b>Fassot C</b>. Sleeve gastrectomy in rodents : impact on metabolic, cardiovascular and hepatic functions of mothers and perinatal consequences. En cours de redaction.          - Payen C, Guillot A, Paillat L, Fothi A, Dib A, Bourreau J, Schmitt F, Loufrani L, Aranyi T, Henrion D, Munier M, <b>Fassot C</b>. Pathophysiological adaptations of resistance arteries in rat offspring exposed in utero to maternal obesity is associated with sex-specific epigenetic alterations. International Journal of Obesity, 2021; 45:1074-1085.</p>		
<p><u>National and international collaborations:</u>          Dr P. Parnet, Phan laboratory, Nantes (microbiota)          Dr T. Aranyi, Medicine Faculty, Budapest University, Hungary (epigenetic analysis and fetal programming)</p>		