# THERESIS TOPIC

<table>
<thead>
<tr>
<th>Subject N° (to be completed by the ED):</th>
<th>FUNDING:</th>
<th>☑ Requested ☐ Acquired</th>
<th>Funding origin:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thesis title: Extracellular Vesicle-borne Protein tyrosine phosphatase 1B and Inflammation in Metabolic syndrome</td>
<td>3 keywords: Extracellular Vesicle Protein tyrosine phosphatase 1B Inflammation</td>
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<td>Unit / team: SOPAM INSERM 1063 Angers</td>
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**Socio-economic and scientific context (approximately 10 lines):**

Obesity and its metabolic resultant dysfunctions such as insulin resistance, hyperglycemia, dyslipidemia and hypertension, grouped as the “Metabolic Syndrome” (MetS), are chronic inflammatory disorders that represent one of the most severe epidemic health problems. MetS is characterised by a low-grade inflammatory state and by endocrine changes. Obesity and its metabolic consequences are often accompanied by atherosclerosis, defined as the formation of plaques in the arteries, which can lead to cardiovascular diseases (CVD) and type 2 diabetes (TZDM). The degree of insulin resistance, hyperglycemia and dyslipidemia appears to be predictive factors, which increases the occurrence of diabetes described in MetS.

**Working hypothesis and aims (approximately 8 lines):**

Our preliminary results indicate that circulating EVs bear PTP1B (EVPTP1B). Of importance is that PTP1B is expressed in circulating EVs and specifically in MetS patients. EVs from MetS patients, in addition to represent predictive factors, may account for specific inflammatory complications increasing the occurrence of diabetes described in MetS. The objective of the present project is to test the hypothesis that EVPTP1B carried by EVs (EVPTP1B) can be targeted in MetS patients.

**Main milestones of the thesis (approximately 12 lines):**

- Detection, characterization and sorting subsets isolations of EVs and especially EVPTP1B in plasma of MetS and non-MetS patients. The size and the concentration of EVs from each patient will be analyzed by transmission electronic microscopy, Western blot, Nanopart analysis (NTA) and flow cytometry.
- Validation of the implication of EVPTP1B in inflammatory response of monocyte/macrophages and adipocytes and their pathophysiological relevance in the course of atherosclerosis. The effects of EV subtypes will be analyzed on monocyte/macrophage phenotypes and function with respect to cytokine releases, and on adipocytes. The influence of EVs on adipocyte differentiation and further function may account for specific inflammatory complications increasing the occurrence of diabetes described in MetS.
- Correlations between EVPTP1B of non-MetS and MetS patients from the NUMEVOX (CHU Angers) cohort with clinical parameters and biological data will be analyzed. Of particular interest is the correlation with individual risk factors such as hypertension, diabetes, hypercholesterolemia in relation with atherosclerosis. The same correlations will be undertaken in mouse models.

**Scientific and technical skills required by the candidate (2 lines):**

- Cellular Biology, Molecular biology, Imaging, Functional studies of vascular function in mice

**3 publications from the team related to the topic (last 5 years):**


**National and international collaborations:**

- Dr. M. Delibegovic, PTP1B et fonction vasculaire, Aberdeen, UK.
- P. M Lopez, central regulation of obesity, Santiago de Compostela, Spain
- P. I. Laher, obesity Vancouver, Canada.