



## **UNRAVELLING THE ROLE OF NAPE-PLD IN OBESITY ASSOCIATED COLON CANCER.**

Tutor: BARBARA ROMANO Co-tutor: FRANCESCA BORRELLI

Acylethanolamides (AEs) are endogenous bioactive lipids that affect a several pathophysiological functions including inflammation and food intake. N-acyl phosphatidylethanolamine-phospholipase

D (NAPE-PLD) is the key enzyme involved in AEs synthesis which its role in colon cancer is undiscovered. NAPE-PLD has a direct association to obesity both clinically and preclinically (Wangensteen et al., Obesity 2011; Everard et al., Nat Comm. 2019). Considering the crucial role of NAPE-PLD in obesity, a risk factor of colon cancer, the project intends to decipher the role of this enzyme from obesity to colon carcinogenesis.

To pursue this main scope, the essential methodology will include:

- i) in vivo studies: induction of colonic tumours in wild type animals compared to mice with a tamoxifen-inducible deletion of NAPE-PLD in intestinal epithelial cells fed or not with a high fat diet; colonic tumours will be also induced in transgenic models of obesity (i.e. db/db mice) in which NAPE-PLD will be pharmacologically modulated.
- ii) Advanced preclinical models: generation of murine colonic organoids derived from the experimental groups described above. Organoids will be studied for their differences in morphology/proliferation capability. Their lipidomic and metabolomic profile will be also profiled.
- iii) Molecular biology techniques matched with the differential gene expression (by RNA-seq) of the human samples collected from colon cancer patients with different BMI. Differences in NAPE-PLD expression will be correlated among the patients populations.

The project complies with the PNNR themes (mission 4) and the pilar thematic “Advanced preclinical models”.