Candidature bourse ciblée pour un meeting

Nom : Ruggiero

Prénom : Sonia

Mail : sonia.ruggiero@curie.fr

Adresse du laboratoire de thèse :
Institut Curie – Centre de Recherche
Translational Research Department
Breast Cancer Biology Group (BCBG)
Hôpital – 1er étage
26 rue d'Ulm 75005 Paris

Directeur(trice) de thèse :
Dubois Thierry

CV au format PDF

https://cfatg.org/wp-content/uploads/2023/09/cvEng_SoniaRuggiero_Sep2023-1-2.pdf

Résumé des travaux présentés lors du meeting

Triple-negative breast cancer (TNBC) is the most aggressive breast cancer subtype, for which finding new therapeutic strategies is still a priority in oncology. A family of enzymes called PRMTs, which methylate arginines on histones and non-histone substrates, emerged as promising therapeutic targets for TNBC. PRMTs play different roles in the cell; for example, they are involved in transcriptional regulation, alternative splicing and immune response. Recent studies revealed that PRMT4, also known as CARM1, regulates autophagy by acting as transcriptional co-activator for TFEB, leading to the expression of lysosomal and autophagy-related genes under stress conditions. We found that CARM1 is overexpressed in TNBC compared to normal breast tissues and is required for the survival of TNBC cell lines, suggesting that CARM1 could be an attractive target for TNBC. To better understand CARM1 functions in TNBC cells, we have characterized its interactome after immunoprecipitation and mass spectrometry analyses. TFG (TRK-fused gene) and ATG9A, which are both involved in the maturation of autophagosomes during autophagy, were found to interact with CARM1 in several TNBC cell lines. I validated these interactions by co-immunoprecipitation experiments. These results suggest that CARM1 may regulate autophagy also in the cytosol, in addition to its nuclear role as a TFEB co-activator. My project now aims to characterize the functional interplay between CARM1, ATG9A and TFG during autophagy in TNBC cells. More specifically, I would like to examine whether CARM1 regulates autophagy particularly during autophagosome maturation, and whether this happens through the interaction and/or the methylation of ATG9A and TFG.
Since autophagy can act as a pro-survival strategy in tumour cells and its inhibition improved the treatment of certain cancers, understanding the role of CARM1 in autophagy could shed the light on novel mechanisms promoting tumour growth in TNBC.

Lettre de motivation

My name is Sonia Ruggiero, I am starting my third year of PhD in the lab of Dr. Thierry Dubois, located in the Translational Research Department at Institut Curie in Paris. The focus of my lab is triple-negative breast cancer (TNBC), which is considered the most aggressive breast cancer subtype and is indeed difficult to treat in the clinics. Cancer has been my main interest since my early career at university: I was fascinated (and terrified at the same time) by the mechanisms that drive malignant transformation in healthy cells, namely how a perfect coordinated cause-effect network would suffer from some external stimuli and suddenly get reprogrammed, leading to disease. I encountered autophagy just recently during my PhD, when I identified as top partners of my protein of interest, the methyltransferase CARM1, two factors implicated in the maturation of

autophagosomes. Since then, my quest has been to understand the link between CARM1, which is upregulated in TNBC, and its putative role in the regulation of autophagy. The support of the CFATG club in attending this conference would allow me to show my work to experts in the field, getting precious feedback and insights for the sake of my project. This meeting would indeed be an unravelling opportunity to talk science with senior researchers but also with my peers, for sure establishing an enriching discussion. I consider myself still quite new at the topic, and for this reason I am very motivated to attend this conference in order to expand my knowledge on this complicated pathway. More specifically, I am impatient to delve into the intricated relationship between autophagy and cancer: their connection looks certainly tricky, since autophagy could be seen either as a way of cancer cells to die, or an extreme attempt for their survival. This said, recent papers showed that autophagy-targeting compounds were able to limit tumor cell growth in different models, pointing out the autophagy machinery as a promising alternative target for anti-cancer combined therapies. Taking part to this scientific event with the support of the CFATG scholarship would definitely allow me to dissect further the scientific questions my PhD project has risen, with the final aim to clarify the molecular link between autophagy and breast cancer.

Présentation orale

Non

Présentation par affiche

Oui