CLOVES SYNDROME COMMUNITY

RESEARCH ROUNDTABLE PRESENTATION SIMPLIFIED

DATE: March 31, 2022

Ana Angulo-Urarte, PhD. (IJC, Barcelona, Spain)

Ana Angulo-Urarte is a MSCA Postdoctoral Fellow in Dr. M Graupera Lab at Josep Carreras Institute (IJC, Barcelona). She obtained her PhD in Biomedicine in 2017 (IDIBELL, Barcelona) studying PI3K signaling during vascular development using murine and zebrafish models. Ana joined the Dr. Huveneers Lab at the AMC (the Netherlands) for a postdoctoral position in 2017 where she delved into the force-dependent dynamics that happens at the endothelial cell-cell contacts and its role in the formation of new blood vessels.

In 2020, she started her current position in the group of Dr. Mariona Graupera to work in PI3K-related congenital disorders. Her work aims to gain physiological and molecular insight into PIK3CA-related overgrowth spectrum (PROS) and address questions concerning when (timing), where (cell linage), who (PIK3CA variant) and how (triggered mechanism) activating PIK3CA variants contribute to the development and severity of PROS. Hopefully, these studies will contribute to define better and even variant-related personalized pharmacological treatments.

Research Simplified Summary:

Dr. Angulo-Urarte presented her ongoing project on PIK3CA variants in PROS. She is studying the mechanisms linking the degree (quantitative) and signalling output (qualitative) of PI3Kα hyperactivation by the different PIK3CA variants to the onset of different PROS. She has chosen the endothelial cells as her main model of study because the vascular compartment is frequently found affected in PROS patients. She presented the collection of patient-derived endothelial cells isolated from vascular malformations that is being generated in Graupera Lab (in collaboration with the clinicians of Sant Joan de Deu Hospital, Barcelona). This tool allows them not only to identify the pathogenic mutation in the endothelial cells but also to use these cells for cellular and molecular studies. Within their current collection there is a battery of patient-derived endothelial cells with identified oncogenic PIK3CA variants. This battery is composed by samples carrying PIK3CA mutations at different spots of the gene (kinase domain, helical domain, C2 domain, P85 binding domain…). These cells will be use to perform phosphoproteomic, epigenomic and transcriptomic studies aiming to decipher the molecular alterations triggered by different PIK3CA variants found in PROS. On the other hand, she has generated new genetically modified mouse lines to express Pik3ca variants such as E726K and C420R, that together with already available lines of hotspot mutations (H1047R and E545K) will allow her to study in vivo the impact the different Pik3ca variants have in the onset and progression of vascular malformations (and other type of lesions).