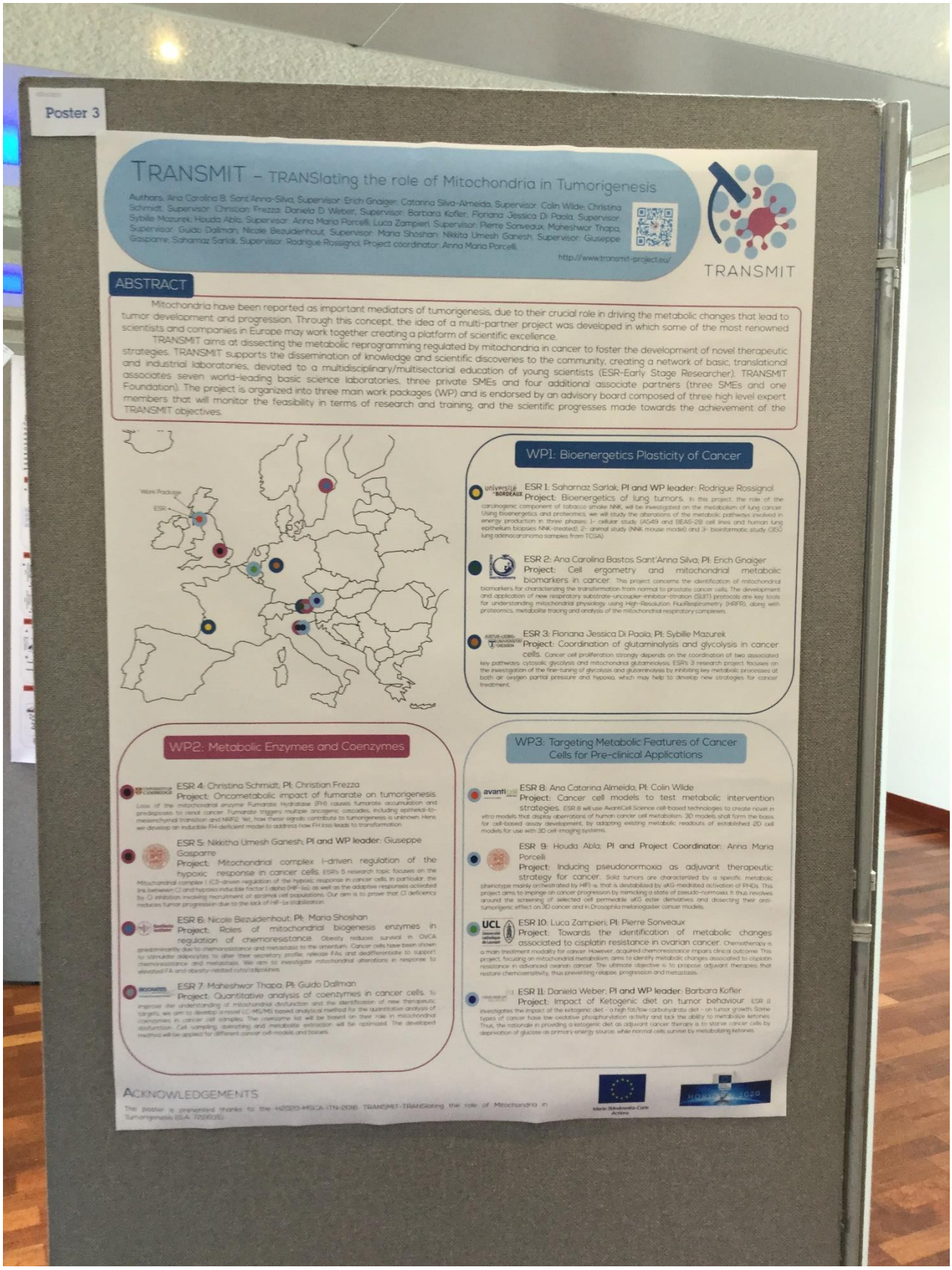
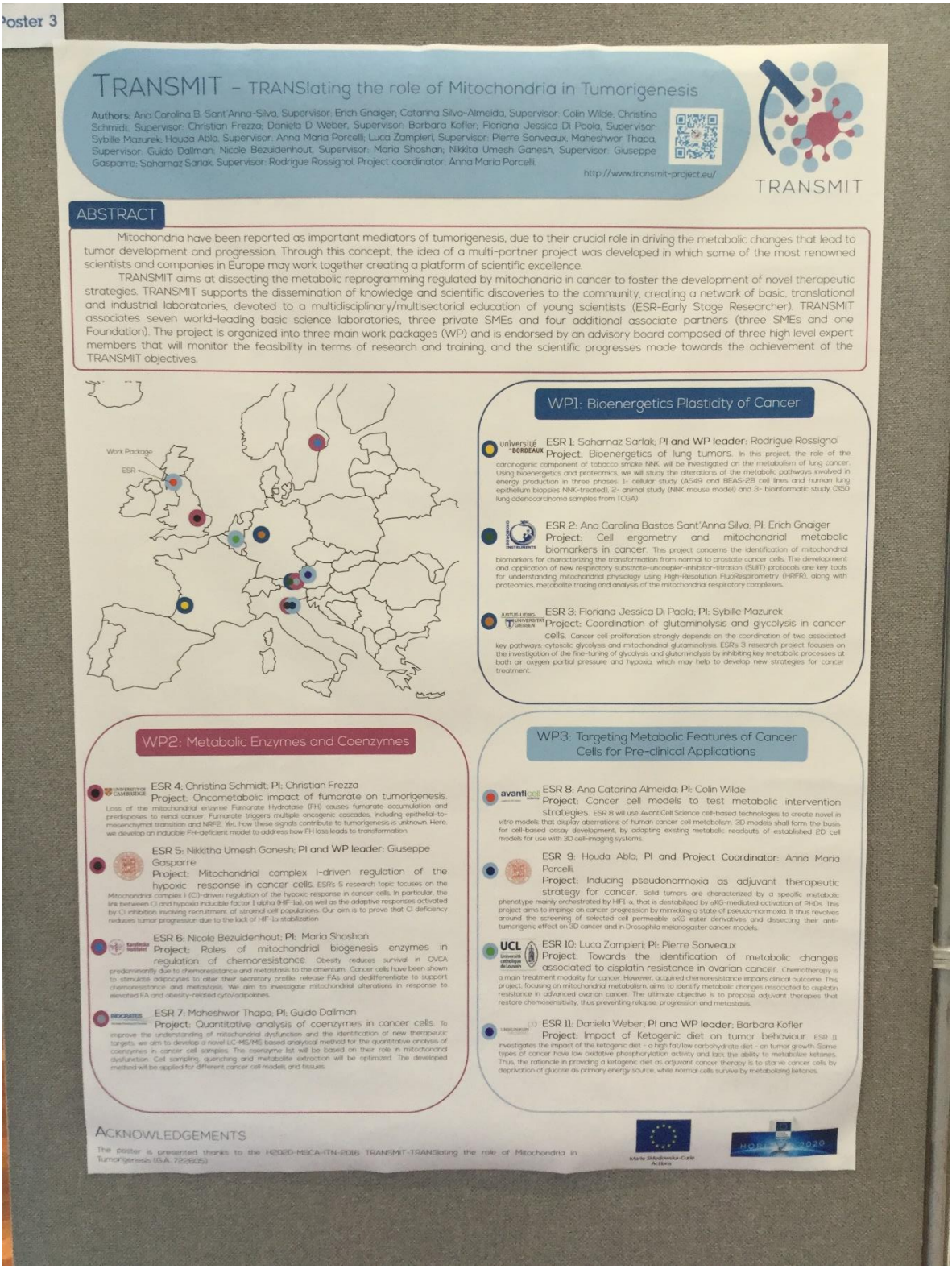

Poster 3
TRANSMIT – TRANSlating the role of Mitochondria in Tumorigenesis
Authors: Ana Carolina B. Sant'Anna-Silva, Supervisor: Erich Gnaiger; Catarina Silva-Almeida, Supervisor: Colin Wilde; Christina Schmidt, Supervisor: Christian Frezza; Daniela D. Weber, Supervisor: Barbara Kofler; Floriana Jessica Di Paola, Supervisor: Sybille Mazurek; Houda Abla; Supervisor: Anna Maria Porcelli; Luca Zampieri, Supervisor: Pierre Sonveaux; Maheshwor Thapa, Supervisor: Guido Dallman; Nicole Bezuidenhout, Supervisor: Maria Shoshan; Nikkita Umesh Ganesh, Supervisor: Giuseppe Gasparre; Saharnaz Sarlak, Supervisor: Rodrigue Rossignol. Project coordinator: Anna Maria Porcelli.
http://www.transmit-project.eu/
TRANSMIT
ABSTRACT
Mitochondria have been reported as important mediators of tumorigenesis, due to their crucial role in driving the metabolic changes that lead to tumor development and progression. Through this concept, the idea of a multi-partner project was developed in which some of the most renowned scientists and companies in Europe may work together creating a platform of scientific excellence.
TRANSMIT aims at dissecting the metabolic reprogramming regulated by mitochondria in cancer to foster the development of novel therapeutic strategies. TRANSMIT supports the dissemination of knowledge and scientific discoveries to the community, creating a network of basic, translational and industrial laboratories, devoted to a multidisciplinary/multisectorial education of young scientists (ESR-Early Stage Researcher). TRANSMIT associates seven world-leading basic science laboratories, three private SMEs and four additional associate partners (three SMEs and one Foundation). The project is organized into three main work packages (WP) and is endorsed by an advisory board composed of three high level expert members that will monitor the feasibility in terms of research and training, and the scientific progresses made towards the achievement of the TRANSMIT objectives.
Work Package
ESR
WP1: Bioenergetics Plasticity of Cancer
ESR 1: Saharnaz Sarlak, PI and WP leader: Rodrigue Rossignol
Project: Bioenergetics of lung tumors.
ESR 2: Ana Carolina Bastos Sant'Anna Silva, PI: Erich Gnaiger
Project: Cell ergometry and mitochondrial metabolic biomarkers in cancer.
ESR 3: Floriana Jessica Di Paola, PI: Sybille Mazurek
Project: Coordination of glutaminolysis and glycolysis in cancer cells.
WP2: Metabolic Enzymes and Coenzymes
ESR 4: Christina Schmidt, PI: Christian Frezza
Project: Oncometabolic impact of fumarate on tumorigenesis.
ESR 5: Nikkitha Umesh Ganesh; PI and WP leader: Giuseppe Gasparre
Project: Mitochondrial complex I-driven regulation of the hypoxic response in cancer cells.
ESR 6: Nicole Bezuidenhout, PI: Maria Shoshan
Project: Roles of mitochondrial biogenesis enzymes in regulation of chemoresistance.
ESR 7: Maheshwor Thapa, PI: Guido Dallman
Project: Quantitative analysis of coenzymes in cancer cells.
WP3: Targeting Metabolic Features of Cancer Cells for Pre-clinical Applications
ESR 8: Ana Catarina Almeida, PI: Colin Wilde
Project: Cancer cell models to test metabolic intervention strategies.
ESR 9: Houda Abla; PI and Project Coordinator: Anna Maria Porcelli
Project: Inducing pseudonormoxia as adjuvant therapeutic strategy for cancer.
ESR 10: Luca Zampieri, PI: Pierre Sonveaux
Project: Towards the identification of metabolic changes associated to cisplatin resistance in ovarian cancer.
ESR 11: Daniela Weber; PI and WP leader: Barbara Kofler
Project: Impact of Ketogenic diet on tumor behaviour.
ACKNOWLEDGEMENTS
The poster is presented thanks to the H2020-MSCA-ITN-2016 TRANSMIT-TRANSlating the role of Mitochondria in Tumorigenesis (GA 722605)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Work Package
ESR
WP1: Bioenergetics Plasticity of Cancer
ESR 1: Saharnaz Sarlak; PI and WP leader: Rodrigue Rossignol
Project: Bioenergetics of lung tumors. In this project, the role of the carcinogenic component of tobacco smoke NNK will be investigated on the metabolism of lung cancer. Using bioenergetics and proteomics, we will study the alterations of the metabolic pathways involved in energy production in three phases: 1- cellular study (A549 and BEAS-2B cell lines and human lung epithelium biopsies NNK-treated), 2- animal study (NNK mouse model) and 3- bioinformatic study (350 lung adenocarcinoma samples from TCGA).
ESR 2: Ana Carolina Bastos Sant'Anna Silva; PI: Erich Gnaiger
Project: Cell ergometry and mitochondrial metabolic biomarkers in cancer. This project concerns the identification of mitochondrial biomarkers for characterizing the transformation from normal to prostate cancer cells. The development and application of new respiratory substrate-uncoupler-inhibitor-titration (SUIT) protocols are key tools for understanding mitochondrial physiology using High-Resolution FluoRespirometry (HRFR), along with proteomics, metabolite tracing and analysis of the mitochondrial respiratory complexes.
ESR 3: Floriana Jessica Di Paola; PI: Sybille Mazurek
Project: Coordination of glutaminolysis and glycolysis in cancer cells. Cancer cell proliferation strongly depends on the coordination of two associated key pathways: cytosolic glycolysis and mitochondrial glutaminolysis. ESR's 3 research project focuses on the investigation of the fine-tuning of glycolysis and glutaminolysis by inhibiting key metabolic processes at both air oxygen partial pressure and hypoxia, which may help to develop new strategies for cancer treatment.
WP2: Metabolic Enzymes and Coenzymes
ESR 4: Christina Schmidt; PI: Christian Frezza
Project: Oncometabolic impact of fumarate on tumorigenesis. Loss of the mitochondrial enzyme Fumarate Hydratase (FH) causes fumarate accumulation and predisposes to renal cancer. Fumarate triggers multiple oncogenic cascades, including epithelial-to-mesenchymal transition and NRF2. Yet, how these signals contribute to tumorigenesis is unknown. Here, we develop an inducible FH-deficient model to address how FH loss leads to transformation.
ESR 5: Nikkitha Umesh Ganesh; PI and WP leader: Giuseppe Gasparre
Project: Mitochondrial complex I-driven regulation of the hypoxic response in cancer cells. ESR's 5 research topic focuses on the Mitochondrial complex I (CI)-driven regulation of the hypoxic response in cancer cells. In particular, the link between CI and hypoxia inducible factor 1 alpha (HIF-1α), as well as the adaptive responses activated by CI inhibition involving recruitment of stromal cell populations. Our aim is to prove that CI deficiency reduces tumor progression due to the lack of HIF-1α stabilization.
ESR 6: Nicole Bezuidenhout; PI: Maria Shoshan
Project: Roles of mitochondrial biogenesis enzymes in regulation of chemoresistance. Obesity reduces survival in OVCA predominantly due to chemoresistance and metastasis to the omentum. Cancer cells have been shown to stimulate adipocytes to alter their secretory profile, release FAs and dedifferentiate to support chemoresistance and metastasis. We aim to investigate mitochondrial alterations in response to elevated FA and obesity-related cyto/adipokines.
ESR 7: Maheshwor Thapa; PI: Guido Dallman
Project: Quantitative analysis of coenzymes in cancer cells. To improve the understanding of mitochondrial dysfunction and the identification of new therapeutic targets, we aim to develop a novel LC-MS/MS based analytical method for the quantitative analysis of coenzymes in cancer cell samples. The coenzyme list will be based on their role in mitochondrial dysfunction. Cell sampling, quenching and metabolite extraction will be optimized. The developed method will be applied for different cancer cell models and tissues.
WP3: Targeting Metabolic Features of Cancer Cells for Pre-clinical Applications
ESR 8: Ana Catarina Almeida; PI: Colin Wilde
Project: Cancer cell models to test metabolic intervention strategies. ESR 8 will use AvantiCell Science cell-based technologies to create novel in vitro models that display aberrations of human cancer cell metabolism. 3D models shall form the basis for cell-based assay development, by adapting existing metabolic readouts of established 2D cell models for use with 3D cell-imaging systems.
ESR 9: Houda Abla; PI and Project Coordinator: Anna Maria Porcelli.
Project: Inducing pseudonormoxia as adjuvant therapeutic strategy for cancer. Solid tumors are characterized by a specific metabolic phenotype mainly orchestrated by HIF1-α, that is destabilized by αKG-mediated activation of PHDs. This project aims to impinge on cancer progression by mimicking a state of pseudo-normoxia. It thus revolves around the screening of selected cell permeable αKG ester derivatives and dissecting their anti-tumorigenic effect on 3D cancer and in Drosophila melanogaster cancer models.
ESR 10: Luca Zampieri; PI: Pierre Sonveaux
Project: Towards the identification of metabolic changes associated to cisplatin resistance in ovarian cancer. Chemotherapy is a main treatment modality for cancer. However, acquired chemoresistance impairs clinical outcome. This project, focusing on mitochondrial metabolism, aims to identify metabolic changes associated to cisplatin resistance in advanced ovarian cancer. The ultimate objective is to propose adjuvant therapies that restore chemosensitivity, thus preventing relapse, progression and metastasis.
ESR 11: Daniela Weber; PI and WP leader: Barbara Kofler
Project: Impact of Ketogenic diet on tumor behaviour. ESR 11 investigates the impact of the ketogenic diet - a high fat/low carbohydrate diet - on tumor growth. Some types of cancer have low oxidative phosphorylation activity and lack the ability to metabolize ketones. Thus, the rationale in providing a ketogenic diet as adjuvant cancer therapy is to starve cancer cells by deprivation of glucose as primary energy source, while normal cells survive by metabolizing ketones.
ACKNOWLEDGEMENTS
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