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| Título del Proyecto | **Setting up and validating improved strategies for the identification and eradication of the poor prognosis fetal-type colorectal tumors (ColoStem-Apply)** |
| Nº de expediente asignado | AC24/00006 |
| Abstract | Work from our consortium published in Nature Communications in 2022, but also supported by recent publications in Cell (Rehman, 2021) and Cell Metabolism (Sun 2023), indicates that fetal/embryonic conversion represents one of the main escape routes of colorectal tumors to chemotherapy, a mechanism that may be shared by other tumor types. In addition, the partners of the consortium identified a fetal gene signature, composed of 28 up- and 8 down-regulated genes, that is present in about 24% of all colorectal cancer patients at diagnosis (which would represent 600,000 cases per year in Europe) and is predictive of poor prognosis, even at early tumor stages II and II+III (ColoStem, protected by patent P5635EP00). In the same publication we have also identified the Hippo/YAP1 pathway as a potential regulator of fetal conversion in cancer and showed that YAP1 inhibitors sensitizes fetal-type patient-derived organoids (PDOs) to the chemotherapeutic agents 5-FU and irinotecan, ultimately leading to efficient tumor eradication.<br>Within this project, we will use fresh tumor tissues and PDOs as well as different OMIC strategies to identify candidate therapeutic targets for the treatment of patients with fetal-type tumors. Integration of the data obtained from these analyses will allow the design of an in vitro medium throughput screening platform (based on PDOs) to validate the vulnerabilities of fetal-type tumors, which will be further confirmed in zebrafish avatars and murine PDX models. We assume that elements of the Hippo pathway will emerge in our analysis, but other potential druggable targets are expected. In addition, the use of PDOs with different mutational backgrounds will provide insight into additional players in fetal transformation in cancer. Our ultimate goal is to develop the first companion diagnostic strategy against fetal-type tumors combining a diagnostic/prescription device (ColoStem) with a personalized treatment (ColoStem-Apply). |
| Entidad Financiadora | Instituto de Salud Carlos III (ISCIII) |

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| Convocatoria: | EP PerMed: Identification or Validation of Targets for Personalised Medicine Approaches (PMTargets) (JTC2024) –<br>ACCIÓN CONJUNTA INTERNACIONAL AC24 – AES 2024 |
| Importe de la ayuda | 300.000 € |
| Fechas de ejecución del proyecto | 01/01/2025 – 31/12/2027 |
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| Enlaces: | https://www.eppermed.eu/funding-projects/projects-results/projectdatabase/colostem-applied/ |