Advanced genomics, design of new animal models and patient sample collection: EDITOR project goals during 2019

- Blood or Leukemia are some scientific journals that have published the scientific advances of this international consortium during its first year

December 2019. EDITOR project, focused on improving early detection and intervention of blood cancers, has completed a year with a positive balance in its forecasts. It started in its kick-off meeting held in January 2019 at Clinica Universidad de Navarra headquarters in Madrid (Spain). During this year the 13 institutions -from Spain, Italy and the United Kingdom- that form part of this international consortium have advanced in the knowledge of monoclonal gammopathies such as multiple myeloma, leukaemia and lymphoma. For that progress, the scientists based the research on the use of the latest techniques in genomic sequencing, the development of new humanized animal models of these diseases, and the compilation of large patient samples.

Among the scientific advances of the project, researchers have implemented protocols for advance genomics. Therefore, they used techniques such as RNA-sequencing or massively parallel single-cell RNA-sequencing based on small cell populations selected through high sensitivity fluorescence-activated cell sorting, a specialized type of flow cytometry. "The results obtained with these techniques are changing our understanding of myelomagenesis and clonal heterogeneity, and that could have an impact on the development of new therapeutic strategies," says Dr Jesús San Miguel, Director of Clinical and Translational Medicine at Universidad de Navarra and the lead investigator.

Also, the researchers have developed mouse models for different malignancies. On the one hand, they established a new genetically modified immunocompetent mouse model that recapitulated the natural history from monoclonal gammopathy of undetermined significance into multiple myeloma. Furthermore, they developed myeloproliferative neoplasm mouse models including an hnRNPK overexpression mouse model to model myeloid malignancies. And they also developed another mouse models of early malignancy in Follicular Lymphoma.

To achieve the project goals, researchers are implementing the sample collection of individuals with this malignancies. By the end of the first year, they have collected more than 3,200 patient samples.

These research results were published in the scientific journals Blood, Leukemia, and Clinical Cancer Research……

Achievements and outputs of the Award to date

In the first 12 months, we have implemented protocols for advance genomics (RNAseq, ATACseq, massively parallel single-cell RNA-seq (MARSeq) based on small cell populations selected through high sensitivity FACs sorting. Results obtained are changing our understanding of clonal heterogeneity, the role of aging and pathogenies in MDS/AML, FL and MM.

We have optimized, fix and perm protocols for rare t(14;18) cell enrichment as well as protocols, including a single cell RNA-Seq (scRNA-Seq) SPLiT-seq workflow compatible with cell fixing and permeabilisation (optimized in B cell lines, primary FL samples

We have standardize MFC protocols for accurate monitoring of immune system and to define immune signatures with impact on disease aotucome

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We have developed a standardized approach *for* quantification, isolation and genetic characterization of CTCs, as a surrogate *for non-invasive risk-stratification of MM and AL patients.*
We have stablished a new genetically modified immunocompetent mouse model that recapitulate the natural history from MGUS into MM, AML and FL

We have developed standardized the protocols for high sensitivity MRD and cell sorting to investigate the genetic fingerprint of chemoresistant cells (both in MM and AML). Our initial data indicate that MRD should be the endpoint of therapy in MM (particularly in high risk patients) and AL.

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We have continued to implement the sample collection of individuals with clonal hematopoiesis (over 2000 samples). .

Regarding ***Computational systems biology for the identification of new targets and development of individualized therapies (WP5): 1.***The data repositories that will be used in the project have been defined (EGA & ENA) and the instructions for creating their Data Access Committees (DAC) have been established***. 2.*** The project website has been released (https://editorproject.com), including an appropriate section for the WP5 results. Its update and maintenance policies have been also established. ***3.***Subprojects within each WP5 group have been defined (at least three in each WP5 group), being some of them already started. ***4.***The contact information of all WP5 bioinformaticians members, including their field of expertise, have been distributed to all groups in order to favor collaborations.