Annual progress report

I. Summary of the context and overall objectives of the project

ImmUniverse aims to advance the understanding of the molecular mechanisms underlying Ulcerative Colitis (UC) and Atopic Dermatitis (AD) by implementing a multi-omics approach using a broad range of molecular profiling techniques to identify signatures of local and circulating biomarkers and mechanistic principles that are informative of disease severity and future disease progression. The overall concept of identifying integrated comprehensive molecular signatures of disease-affected tissue microenvironment ant matched blood biosamples over time will be supplemented with disruptive non-invasive liquid-biopsy methodologies to ultimately reduce the reliance of invasive biopsy methods. ImmUniverse aims to significantly improve immune-mediated inflammatory disease (IMID) management and consequently every patient's life. Following this unique and unparalleled approach, ImmUniverse will fill the gap and the limitations of previous investigational approaches, which did not investigate the complex interactions between circulating immune cells and tissue microenvironment. In addition, due to the parallel study of two different IMIDs, the project will enable the identification of both disease-specific as well as cross-disease signatures and underlying pathological pathways. ImmUniverse will provide a scalable, clinic-ready production infrastructure for delineating the tissue microenvironment and accessible matrices, such as blood and stool, using multiple technologies (single cell sequencing, multi-omics approaches) on several molecular Omics layers.

II. Work performed from the beginning of the project to the end of the period covered by the report and main results achieved so far

Although the overall activities have been significantly delayed by the COVID-19 pandemic situation, the consortium has achieved a major progress, building up the overall IT infrastructure to enable integrative data analysis of both technical, omics datasets and clinical datasets. Clinical partners have prepared the initiation of clinical studies in both UC and AD across multiple sites and patient recruitment at selected sites has commenced. Ethical and regulatory documentation, SOPs and protocols for the different 'omics' layers have been prepared and shared among the partners involved. Both new disruptive non-invasive liquid-biopsy technologies, dOFM and LIPUS, have been launched. SOPs for sample processing and shipment procedures have been prepared. For dOFM ethical and regulatory approval is pending at the clinical sites. The LIPUS studies have been delayed due to the COVID pandemic, but both high and low frequency devices are now fully setup and initial in vitro studies have commenced in preparation for future clinical studies.

III. Progress beyond the state of the art, expected results until the end of the project and potential impact (including the socio-economic impact and the wider societal implications of the project so far)

The ImmUniverse project will bring IMID clinical management to a new level through novel, validated and clinic-ready circulating biomarker assays which are expected (a) to improve diagnosis, (b) to inform early in the clinical course on disease severity and progression and (c) to enable treatment response/remission monitoring. Moreover, implementing disruptive non-invasive liquid-biopsy methodologies will provide significant advances; dOFM has the potential to provide a high resolution signature of the intersitual fluid allowing correlation between tissue and blood and aid in identification of robust circulating signatures in AD, while LIPUS has the potential to induce tissue specific cellular and molecular components into the blood allowing induction of circulating signatures, thereby replacing intestinal biospies. This is particularly relevent for UC as currently, biopsy and endoscopic assessment of mucosal healing are the gold standard for the evaluation of diagnosis and inflammatory bowel disease (IBD) progression. Although well tolerated, both endoscopy and biopsies are invasive, thus limiting their use and frequency, and they do not reflect disease dynamics or sensitivity to the treatment. Traditional biopsy is limited by the quality and amount of the tissue that can be sampled. Similarly, frequency of biopsy sampling in dermatology is a limiting factor. Therefore, there is a high clinical need for robust signatures of the disease tissue microenvironment from blood and/or non-invasive detection methods that could monitor the real-time dynamics of IMIDs. The liquid biopsy represents an alternative and attractive non-invasive procedure. If successful, Immuniverse will provide tissue-specific biomarker signatures that will significantly advance diagnosis, disease prognosis and therapy response, which will be of extreme importance to patients, clinicians and health authorities.

Animated video clip explaining the objectives and approach of the project available on www.immuniverse.eu