PERSIMUNE SCIENTIFIC ANNUAL REPORT 2019

Annual highlights:
One of the major highlights of the research conducted by PERSIMUNE in 2019 was a study that sought to answer the primary PERSIMUNE hypothesis – namely that there is a common pattern of un-discovered risk factors explaining the variation in clinical outcomes – in a large cohort of hospital data from the UK biobank. The results of this study were recently published in Nature Genetics (Cortes A, Albers PK, Dendrou CA et al 2020). In this study, the common pattern of un-discovered risk factors was variation in the host genome (single nucleotide polymorphisms (SNPs)), and the researchers sought to identify SNPs that mediate risk in multiple clinical disease entities (classified using ICD-10 codes). Of particular interest was the observation that SNPs in both the HLA and ABO (Blood Type) region were associated with variety of disease entities, including a number of immune related diseases. This observation is in line with other ongoing PERSIMUNE studies showing that variation in the HLA region is associated with an altered response to HIV (Ekenberg, C, Reekie J, Zucco AG et al 2019) and associated clinical events (Ekenberg C, *submitted manuscript*), as well as an ongoing study exploring the effect of ABO type on risk of clinical outcomes in sepsis patients (*Itenov TS, manuscript under preparation*).

Another highlight of 2019 was work that showcased PERSIMUNE's growing expertise in the field of machine learning. In this study, researchers set out to develop a machine learning based algorithm that could predict the likelihood of patients with chronic lymphocytic leukemia (CLL) developing infection, the results of which were recently published in Nature Communications (Agius R, Brieghel C, Andersen MA et al 2020). Currently, most patients with CLL do not require treatment. However, due to underlying immune dysfunction related to their CLL disease, these patients are at elevated risk of infection. Infections in this population is a significant cause of morbidity and mortality and there is currently no way of predicting which patients are most susceptible to infection. In this study, data from the PERSIMUNE datalake on 4149 patients with CLL was used to develop an ensemble machine learning algorithm that reliably calculated a personalized risk score for a patient developing an infection. The risk score developed as part of this study has been launched as a freely available online clinical application (CLL-TIM.org) and a randomized clinical trial applying CLL-TIM for patient selection has begun to test whether short-term targeting of two putative pathways implicated in CLL interaction with the microenvironment (BTK and bcl-2) can improve immune dysfunction, the PreVent-ACaLL trial (https://clinicaltrials.gov/ct2/show/NCT03868722).

The final highlight of 2019 was PERSIMUNE's ability to build on the initial funding granted by DNRF to secure external funding. In this case, in the field of microbiome research in patients with immune dysfunction. As described later in this report, microbiome research is a strength of PERSIMUNE, and because of this we were recently able to secure funding from the EU Horizon 2020 grant scheme to assess the impact of the microbiome on chronic inflammation and clinical events in people living with HIV across Europe (The MISTRAL study - http://www.irsicaixa.es/en/microbiome-based-stratification-individuals-risk-hiv-1-acquisition-chronic-clinical).). This study is a multi-centre collaborative trial and is the largest study of its kind assessing microbial risk factors of disease in this vulnerable and relevant disease group. In total, this study received ~10 million Euros in funding, with PERSIMUNE researchers to receive a little over 1 million Euros for our role in this study. Participation in this study will solidify PERSIMUNE's place as a leader in microbiome-based research relating to patients with immune dysfunction. This study will also provide us with the opportunity to develop new collaborations and expertise's that will then benefit Danish patients contained within the PERSIMUNE project.

During 2019 55 articles were published. During the first 5 years of its life cycle the centre has produced a total of 162 publications, of which 43 are in A (10 in A+) journals (see annex 1).