A plasma-derived ceruloplasmin from the optimization of plasma fractionation

Plasma-derived proteins play a crucial role in providing life-saving replacement therapies for rare conditions such as primary immunodeficiencies, autoimmune neurological diseases, and coagulation disorders like hemophilia. These proteins also have applications in critical care, such as albumin. Despite the complexity of the plasma proteome, the therapeutic potential of plasma proteins remains largely untapped. Plasma-derived therapeutics, with immunoglobulin and albumin being the most produced examples, are manufactured through an industrial fractionation process. This process involves purifying proteins from individual intermediates, some of which are left unused and discarded. From ethical, economic, and medical standpoints, developing therapeutics from these unused plasma fractionation intermediates would represent a significant innovation. To achieve this goal, we have characterized the proteome of unused plasma fractionation intermediates and identified proteins with potential as new candidate therapies for human diseases. By utilizing bioinformatics and data mining, we have prioritized proteins with the potential to serve as novel protein replacement therapies for rare and orphan conditions. One promising candidate is ceruloplasmin, a plasma ferroxidase that could be used as a therapy for aceruloplasminemia, an adult-onset ultra-rare neurological disease caused by iron accumulation due to ceruloplasmin mutations. Ceruloplasmin, purified from an unused plasma fractionation intermediate, has shown high purity and specific activity, making it suitable for preclinical efficacy studies in animal models modelling human diseases where low or absent ceruloplasmin levels lead to pathology. These findings demonstrate the feasibility of repurposing industrial waste plasma fractions as raw materials for manufacturing new candidate proteins for replacement therapies. This approach not only optimizes plasma utilization but also reduces waste generation, showcasing the potential for innovative advancements in the field of plasma-derived therapeutics.