Gene Expression Profiling: A 'Fishing Expedition' in Search of Dialysis Biocompatibility

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The development of dialysis membranes is closely related to the improvement in hemodialysis as a renal replacement therapy. The main goal to be achieved when designing and improving a hemodialysis membrane is the generation of an efficient and biocompatible filter. Several in vitro and in vivo studies performed throughout the years demonstrated that hemodialysis may induce activation of complement and blood cells such as polymorphonuclear leukocytes, monocytes, or lymphocytes, depending on the membrane material of the dialyzer used. The main analyzed consequence of this activation in the clinical scenario is the evidence of elevated pro-inflammatory cytokines released after stimulation by the bioincompatible membrane material. As a consequence of this blood/membrane interaction, a bioincompatible phenomenon can cause acute and chronic impacts on the dialysis patient; recently, particularly the chronic inflammatory activation gained interest due to the consistent association between systemic inflammation and survival observed in dialysis patients. One limitation of the traditional approach of biocompatibility analysis is the focus on first-line cytokines, such as interleukin-1 and tumor necrosis factor- α , trying to explain a very complex biological process. This process is largely unknown and most likely a result of a cascade of events still to be unveiled.

Therefore, only the recognition and in depth mechanistic analysis of the bioincompatibility phenomenon will allow for the improvement in dialysis membranes. In an article published in this edition of *Blood Purification*, Sohka et al. presented an innovative approach to investigate the complex response of leukocytes after the contact with dialysis membranes. The authors ventured upon a 'fishing expedition', looking for new candidate genes potentially involved in the cellular response to blood/membrane interaction utilizing DNA microarrays.

The information contained in the human genome may be impressive, but without interpretation it remains only a mass of data. Gene function is one of the key elements researchers want to extract from the sequence, and the DNA microarray (also referred to as DNA arrays, DNA chips, biochips and GeneChips) is one of the most important tools at their disposal. The underlying principle is the same for all microarrays, i.e. the unknown sample is hybridized to an ordered array of immobilized DNA molecules whose sequence is known. Each array features thousands of different DNA probe sequences arranged in a defined matrix. Unlike conventional nucleic-acid hybridization methods, microarrays can identify thousands of genes simultaneously, which means that genetic analysis can be done on a large scale and without a previous hypothesis. This has revolutionized the way in which re-

searchers analyze gene expression in cells, allowing researchers to determine which genes are being expressed by a particular cell in a given condition. In the case of the referred study, to determine which genes were expressed by leukocytes in response to contact with particular dialysis membranes. The lack of a hypothesis that characterizes this methodology may lead to unbiased discoveries, which in this case resulted in the identification of urokinase plasminogen activator receptor – CD87 – as a new potential marker to be used in the development of dialysis membranes.

The recent developments in molecular medicine will allow us to quickly advance towards the concept of translational research (from bench to bedside) in the dialysis field. The unbiased gene function discovery provided by DNA microarrays represents an important tool that could be utilized in the future in the development of new dialysis membranes, perhaps increasing membrane biocompatibility and most importantly improving patients' clinical outcome.