## APHERESIS AND TRANSPLANTATION

### Round Table: Organ Perfusion

#### Two voices introduction: the mediators of Organ Damage

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V.F.: Each transplanted organ undergoes a progressive function deterioration, which might culminate in Chronic Graft Dysfunction and is closely linked to acute damage, Primary Graft Dysfunction (PGD) that might be established in the first hours after the transplant. Severe PGD is associated with a worsened graft outcome and an increased risk of recipients' death. This process is mainly linked to ischemia-reperfusion damage, warm and cold ischemia time and oxygen radical production. These conditions induce the release of cytokines, chemokines, complement activation, which cause damage, inflammation, and recruitment of inflammatory cells, already in the intra-operative stage. Also, in the post-operative phases, an important release of inflammatory molecules occurs preluding to the activation of the adaptive immune response. There are also other factors that can intensify the inflammatory response. For example, in marginal organs there is a persistence of bacterial species that can lead to an increase in the release of cytokines and chemokines, therefore, of inflammation in the graft. Moreover, damages during ex vivo perfusion, linked to the ventilation itself, may also occur, especially in lungs. A possible strategy, experimentally tested in our centre, may be the modulation inflammatory mediators by an adsorption technique during ex vivo perfusion, trying to mitigate ischemia-reperfusion injury and, consequently, reducing the risk of short-term and long-term rejection.

G.C.: In the context of ischemia-reperfusion injury, recent evidences have shown that the activation of the complement system and cytokine storm already occur at the moment of brain death of the donor and cover a crucial role in the possible deterioration of the graft function. The main factors involved in this process are mainly C5a and C5b-9. This can lead to a systemic damage during donor maintenance and can affect all organs, not only the kidney, but also the liver and lungs, with chronic effects. In addition to this, the complement system is activated locally and determines the recruitment of granulocytes and monocytes, and above all, can cause irreversible tissue damage. The objective of our treatments is to limit the damage caused by the activation of the complement system and involves several fronts: to act already on the donor and on the recipient, but also to exploit graft preservation techniques using ex-vivo perfusion machines, with the possibility of administer, for example, new drugs to inhibit the complement system, also associating them with an adsorption technique aimed at the modulation of cytokines and C5a.