We congratulate Drs Ündar and Fraser for their results and we appreciate their interest in our article.

As we outlined in our review [1], systemic inflammatory reaction following cardiopulmonary bypass (CPB) is a multi-triggered, multi-factorial, amplified process that leads to leukocytes, endothelial cells and platelet activation and consequent organ dysfunction. Many molecular mediators are involved in the activation of transcription factor nuclear factor kB and certainly the complement system, through its alternate pathway, plays a major role. Dr Ündar and Fraser’s group has used a monoclonal antibody (Mab 166-32) to human factor D to inhibit the alternate pathway of complement activation. In a simulated CPB model using human blood in which blood contact with artificial surface of CPB was the only inflammatory trigger, Mab 166-32 was effective to reduce complement, neutrophil, and platelet activation [2]. Similar results were obtained in a baboon model. Nevertheless, we are anxious to realize whether such promising experimental results will also be obtained in clinical studies: activation of the contact system is not, unfortunately, the only inflammatory trigger. Other authors have obtained significant positive clinical result using single-chain antibody specific for human C5, inducing inhibition of both the classic and alternate complement pathway [3]. Will the complement inhibition achieved by Mab 166-32 be able to produce significant clinical improvements? Hopefully yes but it is hard to answer that question.

It is our opinion that research in this field has been unbalanced towards the treatment of a disease that we do not completely understand yet: we are missing essential insight of the pathophysiology. At this stage of our knowledge we are unable to predict which patients will respond to the operation with an excessive inflammatory reaction, who is going to suffer a significant clinical complication and who, hence, could benefit from a prophylactic treatment (complement inhibition, protease inhibitors, steroids, heparin coated circuits, etc.). Studies in immunology are showing that certain haplotypes have a predisposition towards an excessive reaction of the immune system following stimuli. With a similar inflammatory trigger some subjects develop an excessive inflammatory reaction and for this reason they are considered ‘high responders’ [4]. It is probably among this group of subjects that are those patients that suffer clinical complications related to CPB induced inflammation.

We agree with Drs Ündar and Fraser that cardiotomy suction is a major trigger for inflammation. Moreover, monocyte in blood taken from the pericardium during operation have shown to have increased tissue factor expression leading to the activation of the extrinsic coagulation pathway, thrombin formation and finally impairment of the coagulation system [5]. Ongoing research in our institution will clarify whether the use of cell saver devices, instead of the standard cardiotomy suction, may decrease these effects.

References


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