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LETTER TO THE EDITORS

Extensively burned patients still need blood transfusions and skin allografts: unavoidable HLA sensitization requires optimization of VCA access

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Dear Sirs,

We thank Gaucher and Jarraya [1] for their comments on our study [2]. This first Single Antigen Flow Bead (SAFB) analysis of the strength and breadth of human leukocyte antigen sensitization (supporting information in our study [2]) in extensively burned patients was initiated after facing reduced access to Vascularized Composite Allograft (VCA) transplants for burned candidates. We described its impact on future VCA access and addressed the sensitizing factors and their alternatives. A recent report confirmed this risks of humoral rejection of VCA on sensitized patients [3].

Transfusions are unavoidable in acute care of extensively burned patients. Blood salvage procedures despite feasible have not been widespread due to their poor efficiency/risk (major sepsis) ratio after burns [4]. Red blood cells (RBC) present some HLA molecules that remain a cause of sensitization. In Leffell *et al.*'s study [5] kidney transplant candidates receiving leucoreduced transfusions presented a 20% risk of HLA sensitization versus 2.4% for nontransfused patient. In our study, all burns patients excepted one (not 100% of the patients, as mentioned by Gaucher and Jarraya) were sensitized, with a relative risk to be hypersensitized 3.3 fold higher when compared to kidney transplantation candidates. This could be explained by quantitative differences in RBC transfusions; however, the amounts of RBC received by the kidney transplant candidates were unavailable, as in Leffell's study.

Skin allografts keep a role after extensive burns, provided a risk benefit ratio analysis in the light of a potential VCA indication. Burns surface under or over 70% TBSA are, respectively, led to use CPSA as overlay on skin autograft (widely meshed or micrografted) [6] or for woundbed preparation before application of cultured autologous keratinocytes (CAK) [7]. As overlay, skin xenografts offer comparable efficacy and cost to CPSA [8], while dermal matrix offers poor adherence to CAK. If Kua *et al.* [9] compared glycerol (GPSA) with cryopreserved (CPSA) skin allografts for full-thickness burns, it retrieved no significant difference neither for mortality rates nor for length of stay. Richters *et al.* [10] study reported a very low T-cell response to allogenic glycerol-treated epidermal cells. No immunogenic comparison had been reported between GPSA and CPSA; however, such clinical comparison would require extensive multicentric assessment for a limited clinical relevance. The question of the potentiation between RBC and CPSA would require an animal study.

The transfusion of HLA-matched RBC is not clinically applicable due to the number of units required for the acute care. It requires the development of transfusion components lacking the expression of HLA alloantigens. Skin banks with CPSA stocks allowing for HLA-matched skin grafting are not realistic.

Antibody reductions by desensitization protocols in highly sensitized kidney transplant candidates are not long lasting and frequently recur.

The limited number of patients to survive such extensive burns might limit the development and validation of any HLA sensitization multiparametric score.

Gaucher and Jarraya stated that HLA sensitization must be avoided to keep open the option for VCA. This should be moderated as HLA sensitization do not preclude any VCA transplantation but increase the proportion of potential transplants carrying higher risks of humoral rejection. The priority to life-saving procedures for extensive face or hand burns patients should be combined with effort to reduce their sensitization. Their access to transplants can be optimized significantly by replacing the gender-matching usually applied for VCA by a size/morphological one.

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Conflicts of interest

As principal investigators, Drs. Hivelin and Duhamel had full access to all study data and take responsibility for data integrity and accuracy of analysis. The authors of this manuscript have no conflict of interest to disclose. We hereby certify that no financial support or benefits have been received by any co-author, by any member of our immediate family or any individual or entity with whom or with which we have a relationship from any commercial source which is related directly or indirectly to the scientific work which is reported in the article. We understand an example of such a financial interest would be a consulting relationship or stock interest in any business entity which is included in the subject matter of the manuscript or which sells a product relating to the subject matter of the manuscript.

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