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Biomarkers of tolerance in kidney transplantation: When predicting tolerance adjustment for confounding factors is imperative

We and others have previously described signatures of tolerance in kidney transplantation showing differential-expression of B-cell related genes and relative expansions of B-cell subsets. However, in all of these studies, the index groups namely the tolerant recipients were not receiving immunosuppressive (IS) treatment unlike the rest of the comparator groups. The work will demonstrate that the expression of the previously reported signature was biased by IS regimens, which also influenced transitional B-cells. We have defined and validated a new gene-expression signature that was independent of drug effects and also differentiated tolerant patients from healthy controls and have validated this signature in a number of cohorts. We will demonstrate how adjustment for IS-drug intake does not obliterate the contribution of genes to tolerance, when this exists; but it does indeed remove the effects ascribable to pharmacological immunosuppression and, thus, reveals underlying tolerance characteristics. Consequently, we would argue that IS regimens do affect the expression of many genes (although not all) and require adequate investigation. When IS are, indeed, altering the expression of signature genes, investigators should adjust for IS-drug intake. Only a similar approach will make the conduct of pilot clinical trials for IS-minimization safe, and hence allow critical improvements in kidney post-transplant management.

Biography

Maria Hernandez-Fuentes studied Medicine at Universidad Complutense and then completed PhD in Immunology at Universidad de Alcalá, both in Madrid, Spain. She then moved to the UK, Imperial College London, working on alloimmune responses. In 2005, the research group moved to King's College London and since then she led the biomarker research group of the MRC Centre for Transplantation. She has a long standing interest in understanding and quantifying alloimmune responses and immune monitoring in kidney transplantation; particularly looking at obtaining evidence of tolerance.

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