IMMUNOBIOGRAM a new immunological tool to personalize immunosuppressive therapy in kidney transplant recipients

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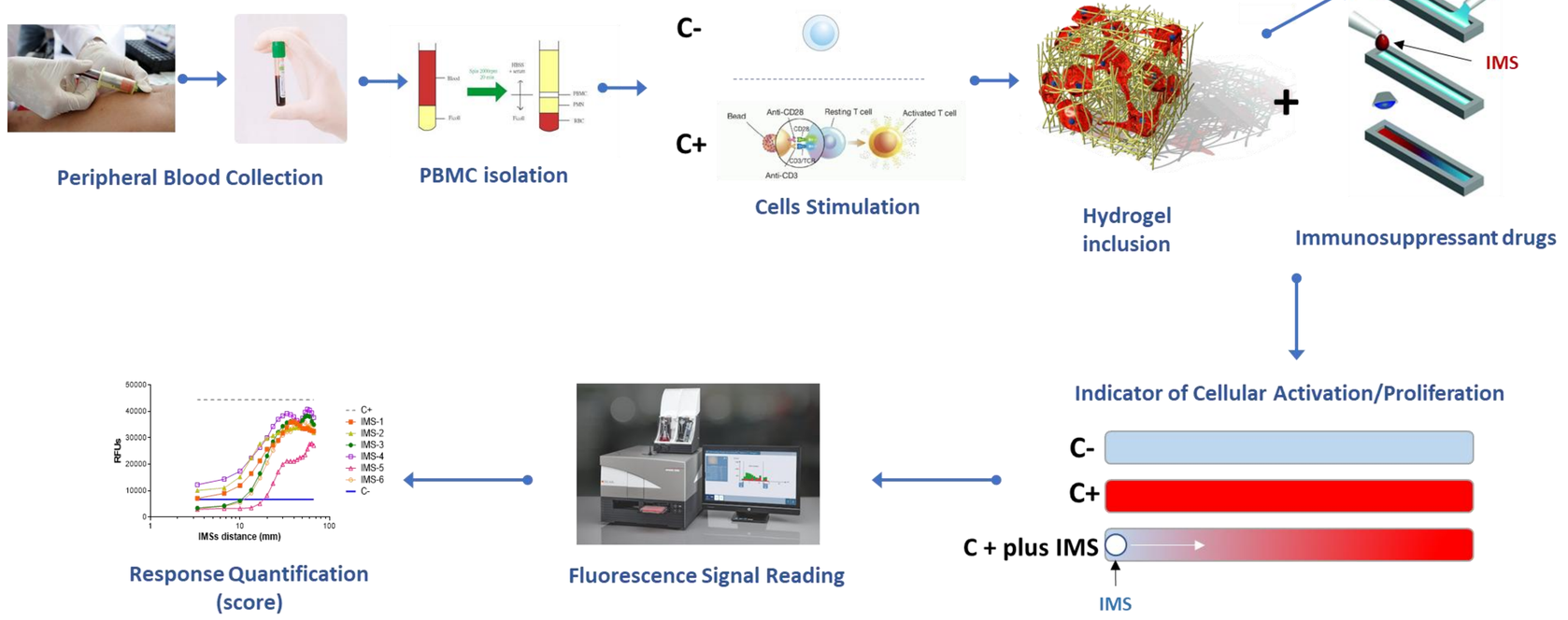
1 Introduction

Persistent risk of organ rejection continues to be a challenge to transplantation. It remains essential to control the immune-mediated tissue specific destruction using immunosuppressive drugs (IMSs) that limit immune system hyperactivation and prevent the allograft loss. IMSs regimens are established based on standard clinical guidelines and empirically. BIOHOPE is developing a blood-based Precision Medicine test for kidney transplantation (KT). It offers a personalized comparative evaluation of patient sensitivity to a panel of immunosuppressive drugs most commonly used. This functional pharmacodynamic and monitoring kit is named Immunobiogram (IMBG)*.

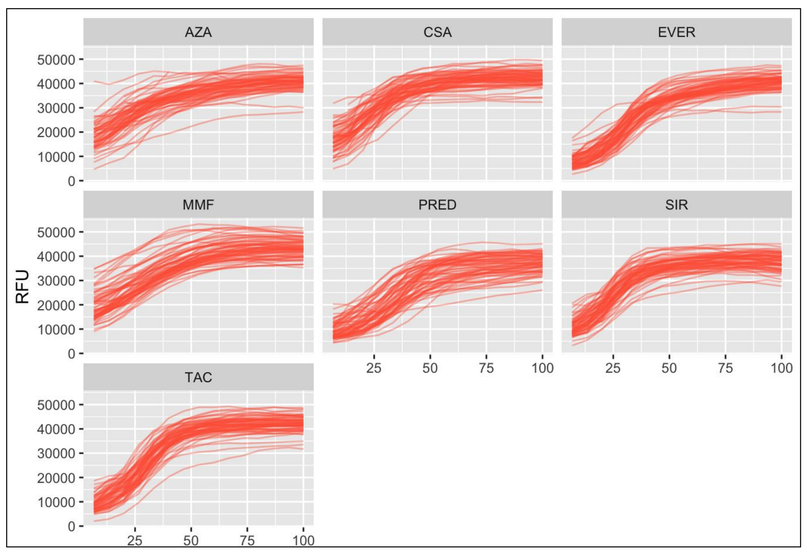
2 Material and Methods

We propose an immunoassay, based on the concept of the antibiogram. This assay is a 3D-cell culture of peripheral blood mononuclear cells included in a hydrogel capable of spontaneous generation of IMSs concentration gradient due to a passive diffusion process. Hydrogel containing cells are loaded in longitudinal channels and IMSs delivery devices are placed in the edge of the channel. After 72 hours of culture, including non-stimulated (C-) and stimulated cells (C+) in the presence or absence of IMSs gradients, an indicator of cell proliferation/viability was used to reveal the capacity of IMSs gradient to inhibit the activation cells state. A quantifiable signal was obtained and properly measured.



3 Results

IMBG was evaluated in BH-pilot study, an observational clinical study performed in two major University Hospitals in Madrid, Spain. It included 70 patients belonging to three immunological risk categories (low-risk, standard and high-risk patients). Seven different IMSs were assayed.



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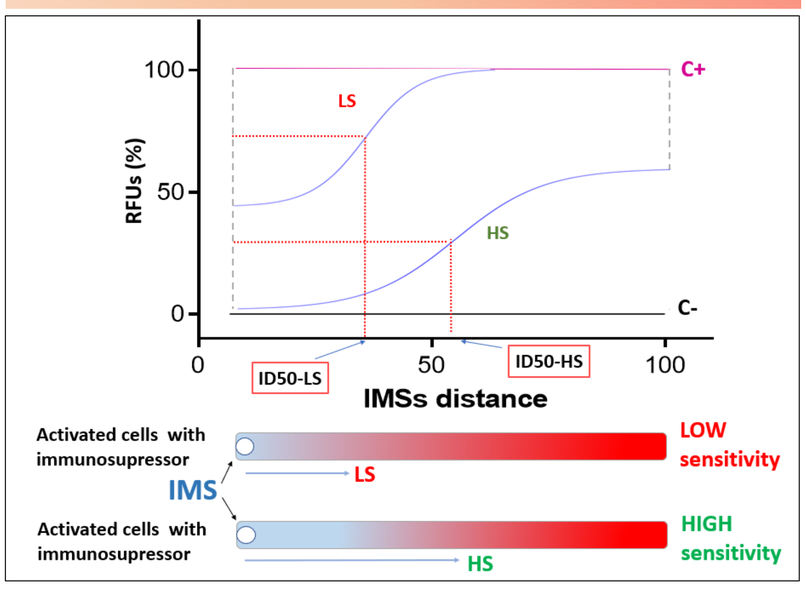
The resulting profiles were used to ascertain the sensitivity of each patient to each IMSs and to establish a panel of IMSs recommendation for the clinical management. Significantly associated low-sensitivity patterns have been observed in patients who present worse clinical evolution. On the contrary, patients with a low-risk profile show better sensitivity scores in IMBG.



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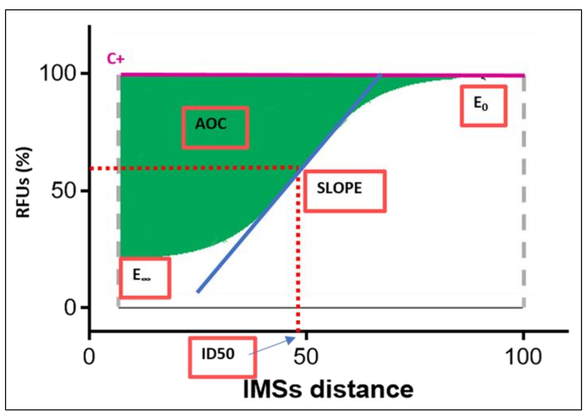
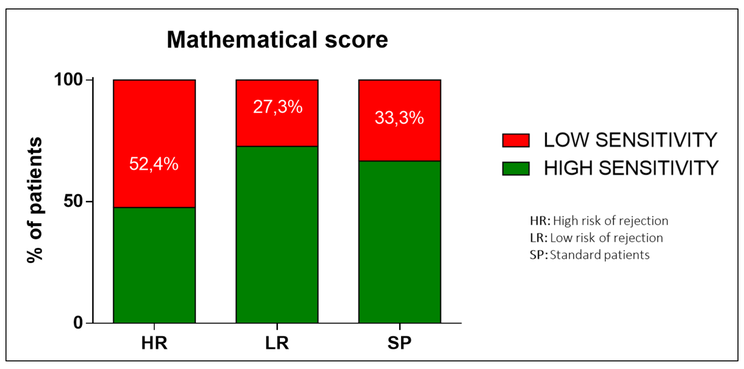
The data generated by the Immunobiogram are represented by IMS through a sigmoid curve and analyzed to generate a score.





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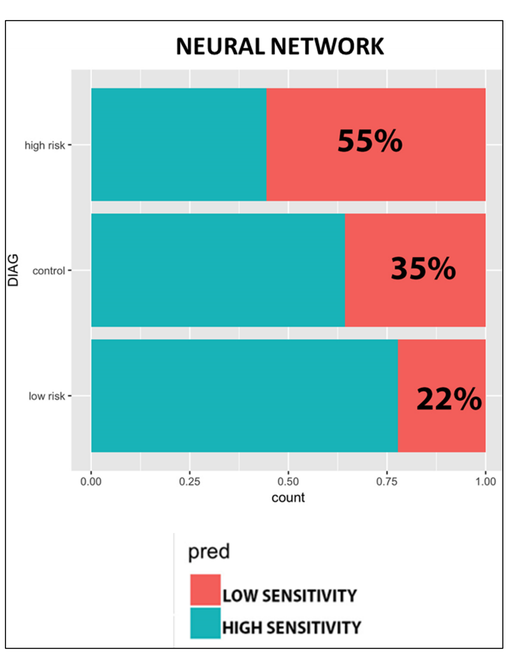
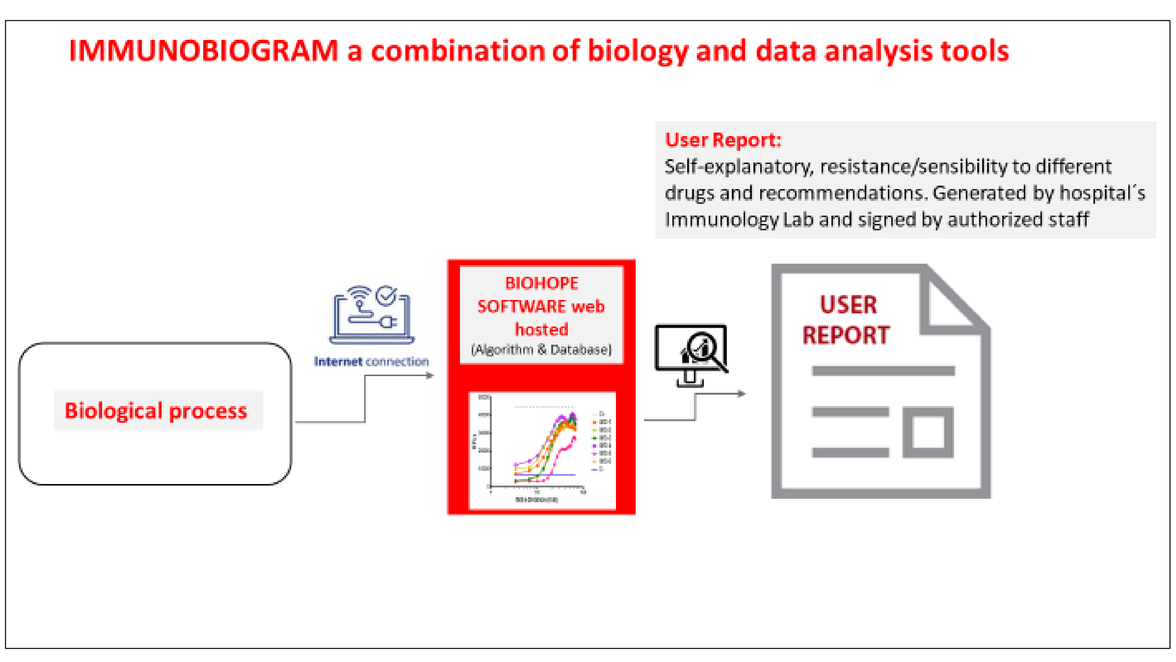
A neural network trained with the 60% of the data and assessed on the remaining 40%, can reproduce accurately and automatedly the results.

The neural network offered as output that more than 50% of clinically high-risk patients could need treatment readjustment.

Based on this approach IMMUNOBIOGRAM can be considered a combination of biological and data analysis tools.





7 Conclusions

The present immuno-assay provides an automatized method to quantitatively measure the response of a patient to immune-modulator drugs that will aid clinicians in the determination of the optimal combination/posology of immunosuppressive/immune-modulator drugs. In addition, this method will open the possibility for clinicians to make the necessary adjustments in immunosuppressive therapy to avoid chronic rejection in KT and reduce side effects of IMSs.

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**Immunobiogram: is a trade mark which belongs to Biohope. Biohope submitted an EU patent application on 2018, June. Coauthors: Javier Dotor, Marianna di Scala, Verónica Sánchez and Isabel Portero.*