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Press release

# EU-TRAIN European study: a step forward in the evaluation of biomarkers in kidney transplantation

**Research teams from the Institut de Transplantation et Régénération d'Organes de l'université Paris Cité (PITOR), the nephrology-transplantation departments of the Saint-Louis and Necker-Enfants Malades AP-HP hospitals, and Inserm, coordinated by Professor Alexandre Loupy, have studied the use of non-invasive biomarkers in monitoring rejection in kidney transplantation. The results of this study were published on August 26, 2024 in the journal *Kidney International.***

Despite considerable therapeutic progress, rejection remains a major cause of kidney graft loss, underscoring the urgent need to improve monitoring and early detection methods. Over the past two decades, a number of innovative biomarkers have shown promising performance in revolutionizing post-transplant monitoring and reducing the number of unnecessary biopsies. However, these biomarkers required rigorous evaluation in international studies specifically designed to determine their clinical utility. This is precisely the aim of the EU-TRAIN (EUropean TRAnsplantation and Innovation) study.

This study has been funded to the tune of 6.6 millions euros over five years by the European Commission as part of the Horizon 2020 program, promoted by AP-HP and supported by Inserm and université Paris Cité. It is made up of 14 partners in five countries (France, Spain, Switzerland, Germany and the UK), including nine European transplant reference centers (Saint-Louis, Necker and Kremlin-Bicêtre AP-HP hospitals, Nantes University Hospital, Barcelona-Vall d'Hebròn, Barcelona-Bellvitge, Berlin-Charité Mitte, Berlin-Charité Virchow and Geneva) and the European Society of Transplantation (ESOT).

The EU-TRAIN study stands out for its innovative methodological approach, designed to meet the specific challenges of real-life biomarker evaluation.

"*For the first time, we conducted a large-scale, prospective, multicenter study, specifically designed to assess the clinical utility of multiple non-invasive biomarkers against parameters used in routine care and without patient selection to favor biomarkers. Furthermore, none of the multiple analytical platforms in the study knew the status of patients at the time of blood biomarker measurements*." Pr Carmen Lefaucheur (PU-PH UPCité - AP-HP), head of the nephrology department at Hôpital Saint-Louis (AP-HP) and Pr Alexandre Loupy (PU-PH UPCité - AP-HP), nephrologist at Hôpital Necker-Enfants Malades AP-HP and director of the Institut PITOR, co-authors of the article.

23 blood biomarkers were studied simultaneously (19 blood messenger RNAs and 4 antibodies targeting non-HLA endothelial antigens) to detect rejection in an unselected cohort of 412 patients who underwent kidney transplantation between November 2018 and June 2020. A total of 812 kidney graft biopsies with concomitant measurement of blood biomarkers were performed in these patients.

Of these, none showed any additional value over standard care parameters (renal function, proteinuria and other clinico-biological parameters) in detecting rejection. These results suggest that these biomarkers may not be generalized for all events and at any time after transplantation and justify their evaluation in specific contexts of use.

*"These results underline the importance of rigorous biomarker evaluation prior to clinical adoption. Our study demonstrates that promising non-invasive biomarkers may not add significant value over standard patient monitoring methods."* Dr Valentin Goutaudier, nephrologist and researcher at the PITOR Institute, first author of the study.

The EU-TRAIN study establishes a new paradigm for transplantation research, and its methodology paves the way for a new era in biomarker evaluation. Its design could be applied to other areas of transplant medicine, and even to other medical specialties, paving the way for the development of new diagnostic and prognostic tools.

"*Our approach offers a robust framework for identifying the right biomarkers of rejection. Better evaluation of candidate biomarkers will improve patient safety and limit research costs for candidates with little or no clinical utility*. "Pr Carmen Lefaucheur.

The results of the EU-TRAIN study have direct and significant implications for clinical practice in kidney transplantation. They provide valuable information to guide clinical decisions and direct future research. This study thus represents an important step towards precision medicine, by establishing rigorous standards for the evaluation and adoption of new biomarkers. It also highlights the importance of international collaboration and research funding from institutions such as the European Commission in advancing transplant medicine.

"*Our results confirm the importance of certain biomarkers already in use, while at the same time urging caution in the adoption of new biomarkers without solid evidence of their clinical utility.*" concludes Pr Carmen Lefaucheur.

***References :*** *Goutaudier V, Danger R, Catar RA, Racapé M, Philippe A, Elias M, Raynaud M, Aubert O, Bouton D, Girardin F, Vicaut É, Yaiche S, Demotes J, Heidecke H, Taupin JL, Randoux- Lebrun C, Zaidan M, Papuchon E, Le Mai H, Nguyen TVH, Moreso F, Berney T, Villard J, Legendre C, Dragun D, Papalois V, Potena L, Giral M, Gourraud PA, Brouard S, Crespo E, Halleck F, Budde K, Bestard O, Loupy A, Lefaucheur C, on behalf of the EU-TRAIN Consortium - Kidney International (2024).*

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