ALLOPIPE: FROM GENOMIC DATA TO MINOR HISTOCOMPATIBILITY ANTIGENS

Adèle Dhuyser, Alice Aarnink, Pierre Delaugere, Pierre Laville, Laurent Mesnard, Hugues Richard

HLA and Histocompatibility Laboratory, CHRU de Nancy; Nephrologic Intensive Care Unit (SINRA), Hôpital Tenon, APHP, Paris; Sorbonne Université Maison des Modélisations Ingénieuries et Technologies (SUMMIT), La Sorbonne Université , Paris; Common and Rare Kidney Diseases (CoRaKiD), UMR 1155 CNRS , La Sorbonne Université, Paris, France
Genome Competence Center MF1, Robert Koch Institut, Berlin, Germany

Recipients transplanted with a genoidentical donor can develop graft-versus-host disease (GVHD) after allogeneic haematopoietic cell transplantation (aHCT), highlighting the contribution of polymorphisms other than those on HLA molecules in triggering alloreactivity. Here, we report on a bioinformatic tool called AlloPipe, which first retrieves the amino acid mismatches within a donor/recipient (D/R) pair from large genomic data - i.e. exome sequencing - and then infer the minor histocompatibility antigens (mHAgs) putatively triggering T-cell activation after aHCT in that D/R pair.

AlloPipe is a stand-alone tool divided into two distinct modules: Allo-Count and Allo-Affinity. Allo-Count compares the genomic data within the D/R pair and compiles the deduced amino acid mismatches into a unique file. If the HLA typing is known, this can be processed by Allo-Affinity to output the immunopeptidome differences within the pair, i.e. the mHAgs. In addition to providing a quantitative score, Allo-Count also reports information about the genomic differences contributing to the score, such as the genomic positions affected or transcript IDs, allowing the user to narrow the score on such parameters if desired. Allo-Affinity additionally retrieves information provided by NetMHCpan, such as the HLA molecules in which the mHAg is predicted to be embedded or its level of affinity towards the HLA molecule. AlloPipe is therefore powerful and flexible and provides insights to better understand alloreactive processes, to better match donors and recipients or to personalise immunosuppressive therapies after transplantation. AlloPipe is open source and available at https://github.com/huguesrichard/Allopipe.

Initially developed in the context of renal transplantation where the occurrence of chronic graft rejection is independently associated with the Allo-Count score (n=53 pairs, previously published), we are currently testing whether this association can be extrapolated to acute or chronic GVHD in the context of aHCT by analysing genoidentical (n=71) and haploidentical (n=40) pairs.