IRICoR
COMMERCIALIZATION OF RESEARCH
Institute for Research in Immunology and Cancer

NEW HUMAN TUMOR-SPECIFIC ANTIGENS IN CANCER IMMUNE-THERAPY

THERAPEUTIC AREA - Cancer immunotherapy

INDICATION - Hematological and solid tumors

OBJECTIVES - To discover MiHAs presented by the most common HLA molecules using a high-throughput mass spectrometry approach and to use them as novel cancer immunotherapy targets

CURRENT STAGE - Target identification

IP STATUS - Pending patent application

PRINCIPAL INVESTIGATORS - *Claude Perreault* (Immunogenetics), *Pierre Thibault* (Proteomics)

COMPETITIVE ADVANTAGES

The strategy used by other groups can only identify TSAs coded by the canonical reading frame of the classic exome. Our strategy enables discovery of TSAs by the entire genome. This is a crucial difference, because most cancer mutations are not in classic exomic sequences.

SCIENTIFIC BACKGROUND AND RATIONALE

A key role of T lymphocytes is to act as extrinsic tumor suppressors and thereby mediate "cancer immunosurveillance". Furthermore, numerous studies have shown that injection of antigen (Ag)-specific T lymphocytes can cure established cancers. Historically, the community has focused on the poorly immunogenic tumor associated antigens (TAAs) that are furthermore derived from genes overexpressed in tumor cells but also present in normal cells. A specific type of Ags can be targeted for T-cell based cancer immunotherapy: tumor-specific Ags (TSAs). TSAs are truly cancer-specific and immunogenic because their presence is induced by cancer-specific somatic mutations.

COMPLETED WORK

Typically, TSA discovery strategies adopt the following path: exome sequencing, identification of mutations, and selection of mutations located in peptide regions predicted to have a good MHC binding affinity. However, when putative TSAs are tested experimentally, by MS or immune assays, the hit rate is below 10%. Furthermore, this approach can only discover TSAs coded by the canonical reading frame of the classic exome. Using a novel proteogenomic, we have found that i) most classic exomic sequences do not generate MHC-associated peptides (MAPs), and that ii) many MAPs are coded by noncanonical transcripts (out of frame exomic sequences and allegedly non-coding sequences).

NEXT STEPS

+ Identification of novel TSAs from mice tumors and validation of their *in vivo* immunogenicity.
+ Discovery of human TSAs in common solid tumors: lung, colon, breast, ovary.
+ Development optimal vaccine with newly identified human TSAs for potential combination with antibodies against immune checkpoint molecules.

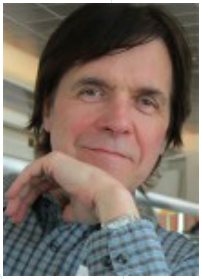
PUBLICATIONS

+ D. Paola Granados, C. Laumont, P. Thibault, C. Perreault The nature of self for T cells - A systems-level perspective Curr Opin Immunol. 2015 Jun;34:1-8.
+ D. Paola Granados, D. Sriranganadane, T. Daouda, A. Zieger, C. M. Laumont, O. Caron-Lizotte, G. Boucher, M.-P. Hardy, P. Gendron, C. Côté, S. Lemieux, P. Thibault, C. Perreault Impact of Genomic Polymorphisms on the Repertoire of Human MHC Class I-Associated Peptides Nature Commun. 2014 Apr 9;5:3600. doi: 10.1038.
+ D.P. Granados, A. Rodenbrock, J.P. Laverdure, C. Côté,, O. Caron-Lizotte, C. Carli, H. Perseon, V. Janelle, C. Durette, E. Bonneil, D.C. Roy, J.S. Delisle, S. Lemieux, P.Thibault, C. Perreault., Proteogeno-based discovery of minor histocompatibility antigens with suitable features for immunotherapy of hematologic cancers. Leukemia, Epub ahead of print February 9, 2016.
+ C.M. Laumont, T. Daouda, J.P. Laverdure, E. Bonneil, O. Caron-Lizotte, M.P. Hardy, D.P. Granados, C. Durette, S. Lemieux, P. Thibault, C. Perreault. Global proteogenomic analysis of human MHC class I-associated peptides derived from non-canonical reading frames. Nat Commun. 2016 Jan 5;7:10238. doi: 10.1038/ncomms10238.

LEAD SCIENTIST

Claude Perreault, M.D., F.R.C.P. (C)

+ Head of the Immunobiology Laboratory, IRIC
+ Full Professor, Dept of Medicine, Faculty of Medicine, UdeM
+ Hematologist, Maisonneuve-Rosemont Hospital (HMR)



Trained as a hematologist, Claude Perreault is one of the founding members of the Institute for Research in Immunology and Cancer (IRIC), the ranks of which he joined as a Principal Investigator in 2005. In addition to his research and training activities at IRIC, Dr. Perreault is a clinical practitioner at Maisonneuve-Rosemont Hospital where he set up both the Histocompatibility Laboratory and the Bone Marrow Transplant Unit. Before joining IRIC, Dr. Perreault worked at the Maisonneuve-Rosemont Hospital Research Center, which he also directed from 1992 through to 2001. Since 2004, he holds the Canada Research Chair in Immunobiology and has recently received the Murray Margarit Memorial Award, Leukemia and Lymphoma Society of Canada in 2009. He has been nominated Fellow of the Canadian Academy of Health Sciences in 2010 and has received the Léo-Pariseau Award from ACFAS in 2011. Claude Perreault and his team at IRIC focus their research initiatives on: 1- The mechanisms responsible for the development of T-lymphocytes; 2- The molecular definition of the immune self and how it is influenced by neoplastic transformation; and 3- The mechanisms of tolerance induction and maintenance by the TGF-beta pathway.

CO-LEAD SCIENTIST

Pierre Thibault, Ph.D.

+ Head of the Proteomic and Bioanalytical Mass Spectometry Laboratory, IRIC
+ Full Professor, Dept of Chemistry, UdeM
+ Accredited Member, Dept of Biochemistry, UdeM
+ Adjunct Professor, Dept of Anatomy, McGill Universitytomy, McGill University

Prior to joining IRIC in 2004 as a founding member, Pierre Thibault was an executive director of the protein analysis department at Caprion Pharmaceuticals (2001-2004) where he developed an industrial scale proteomics platform and novel approaches to the identification of trace-level protein targets for cancer immunotherapy resulting in numerous R&D contracts and partnerships with companies such as Biogen Idec, Abbott and Wyeth. Pierre Thibault was also Research Officer with the National Research Council of Canada's Institute of Marine Biosciences in Halifax (1990-1996) and Institute of Biological Sciences in Ottawa (1996-2002) respectively. He won the National Research Council of Canada (NRC) President's Award for his exceptional contribution to bioanalytical mass spectrometry, as well as the NRC's Outstanding Merit Award for his innovative work in the development of separation techniques coupled with electrospray ionization methods and their applications in protein chemistry and cell biology. Since 2004, he holds the Canada Research Chair in Proteomics and Bioanalytical Spectrometry. He brings his combined expertise in chemometrics, bioanalytical MS and protein chemistry to the development and implementation of new technologies in proteomics and cell biology.

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