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Effect of PTPN22 on Treg to Teff equilibrium in human and murine autoimmune diabetes

Fact Sheet

Project Information

PTPN22 IN T1D

Grant agreement ID: 276745

Project closed

Start date

1 April 2011

End date

31 March 2015

Funded under

Specific programme "People" implementing the Seventh Framework Programme of the European Community for research, technological development and demonstration activities (2007 to 2013)

Total cost

€ 100 000,00

EU contribution

€ 100 000,00

Coordinated by

OSPEDALE SAN RAFFAELE SRL

 Italy

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Objective

"Type 1 diabetes (T1D) is a chronic inflammatory disease, where predisposing genetic factors along with environmental influences result in loss of immunological tolerance and destruction of insulin-producing beta cells. Genetic studies have identified three main T1D susceptibility loci, the human leukocyte antigens (HLA), insulin and most recently PTPN22, which encodes for Lyp/Pep, a lymphoid tyrosine phosphatase. A single nucleotide polymorphism (SNP) in PTPN22 at codon 620 leads to one amino-acid substitution, Arg to Trp (R620W), associated with an increase in T1D risk. A perturbation in the effector (Teff) to regulatory T cell (Treg) equilibrium seems to be implicated in T1D and most cases of autoimmunity. Functional analysis in individuals carrying the R620W polymorphism indicate a "gain of function mutant" resulting in reduced TCR signaling. However, it is not currently known how PTPN22 is involved in mediating T1D susceptibility: effects on Treg and/or Teff thymic selection and peripheral homeostasis may be responsible. Understanding the mechanisms involved could be a key to our understanding of T1D pathogenesis. In addition, strategies that directly target Teff or Treg by inhibiting signaling from PTPN22 could be successful in halting T1D progression. The goal of this project is to analyze the role of PTPN22 on Treg and Teff equilibrium in (pre)diabetic human individuals and selected mouse models of T1D. The specific aims of this Marie-Curie RIG are: 1. Define the role of PTPN22 (R620W allele) on Treg and Teff cells in healthy versus (pre)diabetic individuals, and 2. Determine the role of PTPN22 signaling on Teff and/or Treg in two well-characterized murine models of T1D, (virally-induced [RIP-LCMV] and spontaneous [NOD]). Objectives to be achieved: 1. Functional characterization of PTPN22 mutation on Treg and Teff cells in (pre)diabetic human individuals. 2. Dissection of PTPN22 signaling in selected murine models of T1D crossed to Lyp/Pep deficient mice."

Fields of science (EuroSciVoc)

[medical and health sciences](#) > [health sciences](#) > [inflammatory diseases](#)

[medical and health sciences](#) > [clinical medicine](#) > [endocrinology](#) > **[diabetes](#)**

[natural sciences](#) > [mathematics](#) > [pure mathematics](#) > [mathematical analysis](#) > **[functional analysis](#)**

[natural sciences](#) > [biological sciences](#) > [genetics](#) > **[nucleotides](#)**

[medical and health sciences](#) > [basic medicine](#) > [physiology](#) > **[homeostasis](#)**



Programme(s)

[FP7-PEOPLE - Specific programme "People" implementing the Seventh Framework Programme of the European Community for research, technological development and demonstration activities \(2007 to 2013\)](#)

Topic(s)

[FP7-PEOPLE-2009-RG - Marie Curie Action: "Reintegration Grants"](#)

Call for proposal

FP7-PEOPLE-2010-RG

[See other projects for this call](#)

Funding Scheme

[MC-IRG - International Re-integration Grants \(IRG\)](#)

Coordinator



OSPEDALE SAN RAFFAELE SRL

EU contribution

€ 100 000,00

Total cost

No data

Address

VIA OLGETTINA 60

20132 Milano

Region

Nord-Ovest > Lombardia > Milano

Activity type

Private for-profit entities (excluding Higher or Secondary Education Establishments)

Links

[Contact the organisation](#)  [Website](#) 

[Participation in EU R&I programmes](#) 

[HORIZON collaboration network](#) 

Participants (1)



FONDAZIONE CENTRO SAN RAFFAELE DEL MONTE TABOR 

 Italy

EU contribution

€ 100 000,00

Address

Via Olgettina 60

20132 MILANO 

Region

Nord-Ovest > Lombardia > Milano

Activity type

Research Organisations

Links

[Contact the organisation](#)  [Website](#) 

[Participation in EU R&I programmes](#) 

[HORIZON collaboration network](#) 

Total cost

No data

Last update: 5 April 2023

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