We are not all type 1 diabetic, but we are all 'auto-immune'!

A collaborative study of the INSERM Laboratory led by Dr. R. Mallone (Cochin Institute, Paris, France) and of the French ImMaDiab Study Group in the frame of the international networks INNODIA and nPOD has described the features of the white blood cells associated with type 1 diabetes (T1D). Their discoveries change our understanding of T1D mechanisms and suggest novel therapeutic strategies to halt this disease.

T1D is caused by the destruction of pancreatic β cells that produce insulin, which is the hormone that controls blood glucose levels. This destruction is due to a so-called 'auto-immune' process, i.e. the abnormal recognition of self β cells by the immune system. **A white blood cell subset called 'cytotoxic CD8+ T lymphocytes' attacks β cells by recognizing some protein fragments derived from them.** Despite its increasing frequency (+4% per year in the Western world), T1D treatment is today limited to replace the insulin that is not anymore produced by β cells through multiple daily injections, because **we do not know how to intervene on the immune causes of β-cell destruction**.

Due to their rarity in the blood, the **features of these killer auto-immune CD8+ T lymphocytes** are **poorly understood**. To their surprise, the scientists observed that these lymphocytes **circulate in similar numbers in the blood of all individuals, both T1D and healthy**. Moreover, they display a naive profile, meaning that they are potentially harmful but in a **resting state, because they have not yet encountered their β-cell targets**.

These observations reflect two phenomena. First, the majority of auto-immune T lymphocytes were thought to be eliminated during their development by transiting through the thymus, a specialized organ which presents β-cell protein fragments and kills them on the spot if these fragments are recognized. The scientists have shown that, while **the thymus is not capable of presenting all β-cell fragments**, their presentation or lack thereof **does not impact their elimination**.
Second, **the fraction of T lymphocytes actively engaged in the auto-immune process is sequestered in the pancreas target organ**, where these lymphocytes are found more abundantly in T1D patients compared with healthy individuals.

These results open several questions. **Why do we need to be auto-immune?** This is the compromise needed to be **better protected from infections**, because the auto-immune T lymphocytes spared by the thymus are also capable of attacking microbial protein fragments that are similar to those of β cells. The authors have documented an example of this 'cross-recognition'.
But if we are all auto-immune, why then we are not all diabetic? Two possibilities are under investigation. The first one is that **non-diabetic individuals may be capable of keeping auto-immune T lymphocytes under control**. This control could instead be **lost in T1D patients due to an inflammation of the pancreas**, which may attract the auto-immune T lymphocytes that we all harbor and make β cells more 'visible' to them.

The **next challenges** are to better understand the **ingredients that transform the 'benign' auto-immunity of Mr. Average into T1D**. Identifying these ingredients will allow to **diagnose T1D earlier** and to develop **therapies** to revert auto-immunity to its benign state.