# GENE EXPRESSION PROFILES IN CD4+ T CELLS SUGGEST AN INTERFERON ALPHA SIGNATURE IN CHRONIC ANTIBODY-MEDIATED REJECTION (CAMR) OF KIDNEY TRANSPLANTATION

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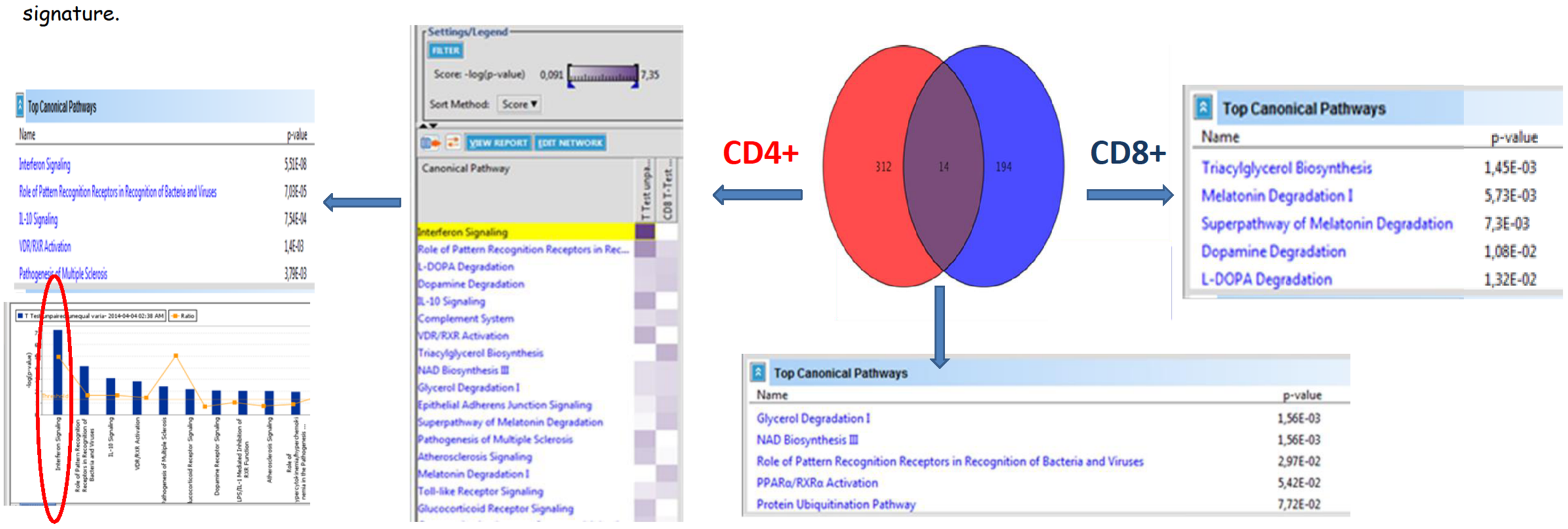
## BACKGROUND AND AIM

- ✓ CAMR is the main cause of chronic graft injury and subsequent graft loss, but its pathogenesis is still largely unclear.
- ✓ The aim of the present study was to investigate the molecular mechanisms underlying the development of CAMR by the analysis of gene expression profiles of both total peripheral lymphomonocytes (PLM) and isolated CD4+ and CD8+ T lymphocytes.

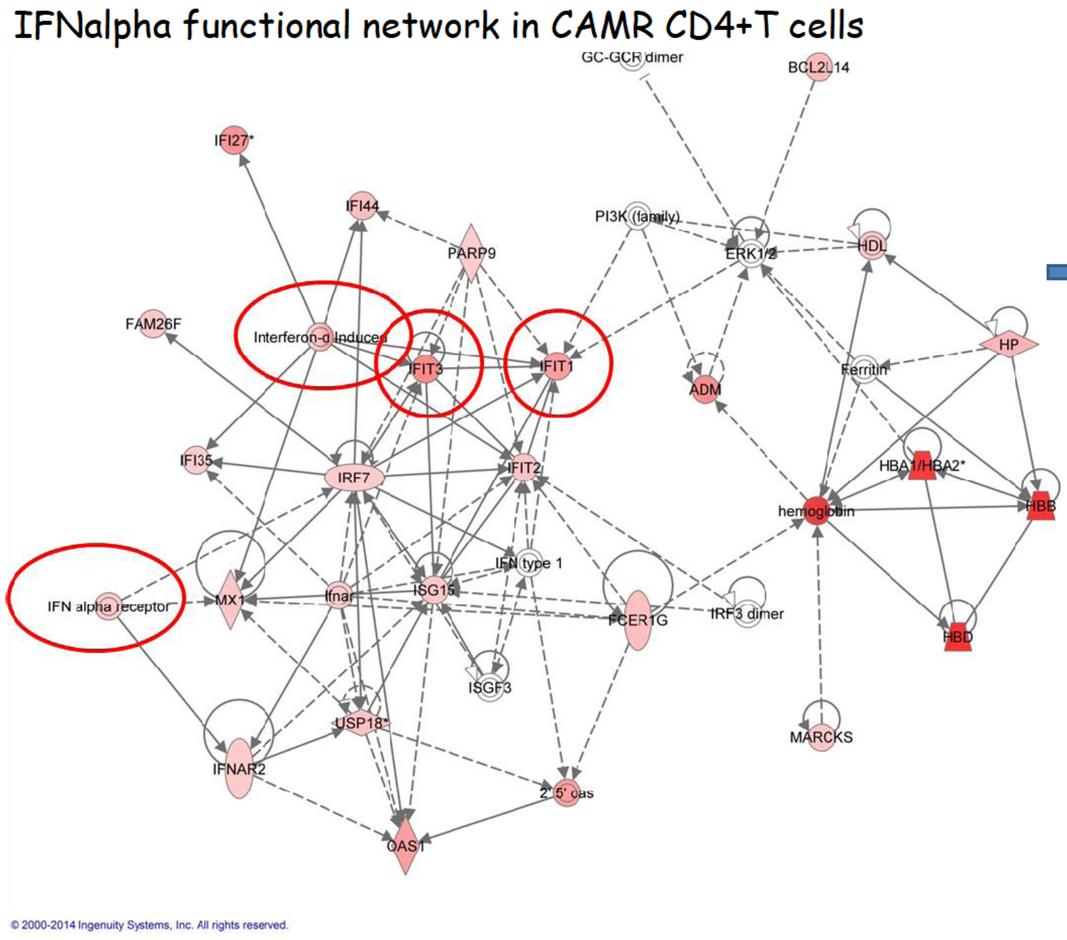
## RESULTS

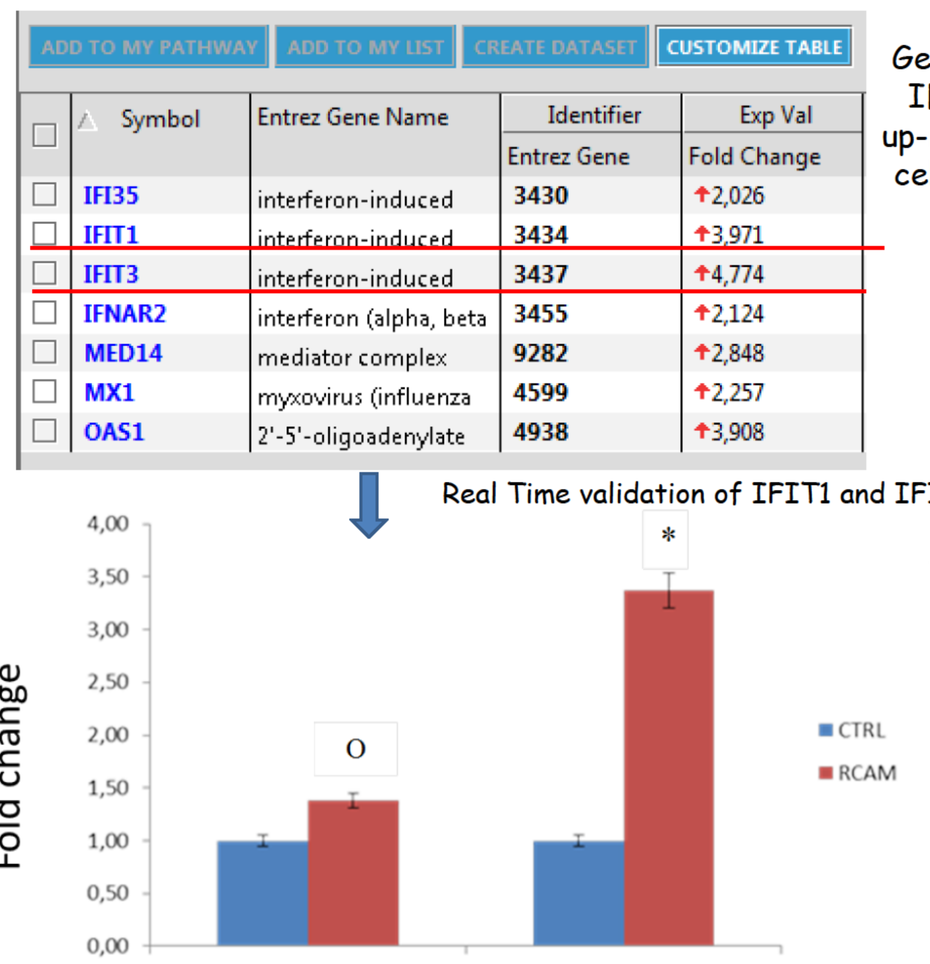
- ❖ 14 patients with biopsy-proven CAMR and 12 stable transplant recipients with normal graft histology and function (control group) were enrolled to perform gene expression profiles of total peripheral lympho-monocytes and isolated CD4+ and CD8+ T lymphocytes by Agilent microarrays.
- ❖ Gene expression profiles of total peripheral lympho-monocytes identified a characteristic activation of the interferon (IFN)-alpha pathway in CAMR patients.
- ❖ The IFNalpha feature was a specific characteristic only of isolated CD4+ T cells, while the gene expression profiles of CD8+ T cells resulted completely distinct.
- ❖ Real time PCR confirmed the differential expression in CD4+ T cells of CAMR patients of genes such as IFIT1 and IFIT3 involved in the IFNalpha signature.




## CD4+ T cells showed a specific IFNalpha feature in CAMR patients vs controls

IFNalpha functional network in CAMR CD4+T cells




Genes involved in the IFNalpha pathway, up-regulated in CD4+T cells of CAMR pts vs CTRL

Real Time validation of IFIT1 and IFIT3 in CD4+ T cells




°p≤0,05 vs CTRL
*p≤0,01 vs CTRL

## CONCLUSIONS

- ➢ Our data suggest a key role for IFN-alpha in modulating the immune response during CAMR, mainly influencing CD4+ T cells response.
- ➢ This observation may open new perspectives for early non-invasive diagnosis of CAMR and to define new therapeutic targets of this serious complication of renal transplantation.

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