LEPTIN RECEPTOR EXPRESSION ON T LYMPHOCYTES MODULATES CHRONIC INTESTINAL INFLAMMATION IN MICE

GIAMILA FANTUZZI

UNIVERSITY OF COLORADO HEALTH SCIENCES CENTER, DENVER, CO
LEPTIN

- 16 kDa PROTEIN
- MAINLY PRODUCED BY ADIPOSE TISSUE
- LEPTIN LEVELS DIRECTLY CORRELATED TO THE ADIPOSE MASS
LEPTIN AS A MASTER HORMONE

LEPTIN EXERTS A TONIC CONTROL ON:

- APPETITE AND ENERGY EXPENDITURE
- GLUCOSE AND FAT METABOLISM
- ADRENAL AND THYROID FUNCTION
- BONE MASS
- REPRODUCTION
- SYMPATHETIC NERVOUS SYSTEM ACTIVITY
- BLOOD PRESSURE
- IMMUNE RESPONSE
LEPTIN-DEFICIENT MICE ARE PROTECTED IN MODELS OF AUTOIMMUNE DISEASES

- INFLAMMATORY BOWEL DISEASE
- T CELL-MEDIATED HEPATITIS
- EAE
- CIA

WHICH CELLS ARE RESPONSIBLE FOR THE IMMUNE-MODULATING EFFECTS OF LEPTIN?
COLITIS INDUCED BY TRANSFER OF CD4⁺ CD45RB<sup>high</sup> CELLS INTO scid MICE

**ENRICHMENT OF CD4⁺ CELLS**

**SORTING**

CD4⁺ CD45RB<sup>high</sup> → 4x10⁵ → scid → AUTOIMMUNE COLITIS
BOTH CD45RB$^{\text{high}}$ AND CD45RB$^{\text{low}}$ CELLS EXPRESS LEPTIN RECEPTORS
EFFECT OF SELECTIVE LEPTIN RECEPTOR DEFICIENCY ON CD45RB<sup>high</sup> LYMPHOCYTES IN COLITIS INDUCTION

WT → CD45RB<sup>high</sup> → scid → AUTOIMMUNE COLITIS

db/db → CD45RB<sup>high</sup> → ?
REDUCED EARLY DISEASE IN *scid* MICE RECEIVING *db/db* CELLS:

SURVIVAL

![Graph showing survival rates of scid Mice receiving db/db cells. The graph compares the cumulative survival rates of scid Mice (red squares) and wild-type (yellow squares). The x-axis represents weeks, ranging from 0 to 12, and the y-axis represents cumulative survival, ranging from 0 to 1. The graph demonstrates a higher survival rate for the scid Mice compared to the wild-type mice.]
REDUCED EARLY DISEASE IN *scid* MICE RECEIVING *db/db* CELLS:

DISEASE SCORE
REDUCED EARLY DISEASE IN scid MICE RECEIVING db/db CELLS:
HISTOLOGIC SCORE
REDUCED EARLY APOPTOSIS IN LPL OF \textit{scid} MICE RECEIVING WT BUT NOT \textit{db/db} CELLS

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\includegraphics[width=\textwidth]{balbc}
\caption{Balb/c}
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\includegraphics[width=\textwidth]{wt}
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\caption{db/db}
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REDUCED EARLY PRODUCTION
OF PROINFLAMMATORY CYTOKINES
IN LPL OF scid MICE RECEIVING db/db CELLS
REDUCED IFN\(\gamma\) PRODUCTION IN FRESHLY ISOLATED \(db/db\) CD45RB\(^{\text{high}}\) CELLS
UPREGULATION OF PPARγ IN THE COLON OF *scid* MICE RECEIVING *db/db* CD45RB<sup>high</sup> CELLS
SELECTIVE LACKING OF LEPTIN RECEPTORS ON T LYMPHOCYTES CONFERS EARLY PROTECTION IN THE TRANSFER MODEL OF COLITIS

- REDUCED PRODUCTION OF PROINFLAMMATORY CYTOKINES
- MAINTENANCE OF HIGH LEVELS OF APOPTOSIS IN LPL
- REDUCED PRODUCTION OF IFN\textsubscript{γ} FROM CD45RB\textsuperscript{HIGH} CELLS
- INCREASED EXPRESSION OF PPAR\textsubscript{γ}