LFA-1/ICAM-1 ligation in T-cells influences both Notch and TGF-β pathways

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T-cell migration into inflamed tissues

T-cell migration in health and diseases

Regulated T-cell migration

Immune response regulations

Uncontrolled T-cell trafficking

Chronic inflammatory diseases
Laboratory model of T-cell migration

Resting T-cells

LFA-1

ICAM-1

Migrating T-cells

Receptor activation

LFA-1/ICAM-1: changes in gene expression

Verma et al. (2012) J Biol Chem
LFA-1/ICAM-1 up-regulates both TGF-β inhibitory molecules and Notch signalling proteins (verified by RT-qPCR)

- **SMAD7**
- **SMURF2**
- **SKI**
- **SKIL**
- **NOTCH1**
- **JAG1**
- **JAG2**
- **HEY1**

TGF-β pathway

Notch pathway

*Verma et al. (2012) J Biol Chem*
Notch Pathway: LFA-1/ICAM-1 activates Notch signalling

- LFA-1/ICAM-1 activates Notch signalling
- ICAM-1
- Jag1
- ICAM-1
- Jag1 + DAPT
- ICAM-1 + DAPT

Unpublished data
LFA-1/ICAM-1 activates Notch signalling
LFA-1 regulates Notch via Akt/ERK/GSK3β signalling axis.
LFA-1/ICAM-1 favors Notch-dependent Th1 polarization

Unpublished data
Notch Pathway summary

Notch signalling pathway

ICAM-1 → Notch receptor → LFA-1

DAPT → NICD

γ-secretase

GSK3β

CoA → p300

CSL

Th1 Polarization
TGF-β pathway: LFA-1/ICAM-1 up-regulates TGF-β inhibitory molecules

Inhibition of IL-2 secretion & chemotaxis
T-cell differentiation

Verma et al. (2012) J Biol Chem
LFA-1/ICAM-1-induced TGF-β inhibitory pathway is dependent on STAT3 and/or JNK
LFA-1 stimulated T-cells are refractory to iTreg or Th17 differentiation

**Th17**

Verma et al. (2012) J Biol Chem
Summary: LFA-1/ICAM-1 induced TGF-β refractoriness in T-cells

LFA-1/ICAM-1 signalling

- ICAM-1
- LFA-1
- STAT3
- JNK
- AP-1
- SMAD3
- SMAD2
- SMAD7
- SKI
- SMURF2

TGF-β signalling

- TGF-β
- TGF-β receptor
- SMAD3
- SMAD2
- SMAD7
- SMURF2
- SKI

Inhibition of IL-2 secretion, Th17, iTreg
Funding support

Laboratory members

Existing collaborations

REDEFINING MEDICINE, TRANSFORMING HEALTHCARE

THANK YOU!