Role of Maraviroc and/or Rapamycin in Interleukin 10 Knockout Frail Mice Model

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Introduction

• As age increases, the risk of developing fragility also increases.

• Frailty is a syndrome characterized by a state of increasing vulnerability, decreased physical function, and adverse outcomes.

• Interleukin (IL)-10 homozygous knockout mice (IL10KO) constitute an excellent tool for the study of frailty.

• CCR5 mRNA expression is overexpressed in patients with frailty.

• Rapamycin (RAPA) has antiproliferative properties and it is also able to decreases CCR5 mRNA expression.

• So far, only one specific CCR5 antagonist is currently approved for clinical use, maraviroc (MVC).

• **Objective**: to evaluate the effects of MVC and/or RAPA in an experimental mouse model of frailty.
Methods

Control group

MVC

IL10KO
(n = 80)

24w

RAPA

MVC + RAPA
Results (I)

- **Percent survival (%)**
  - Control
  - MVC
  - RAPA
  - MVC+RAPA

- **Days**
  - 0, 28, 56, 84, 112, 140, 168

- **AST (IU/L)**
  - Control
  - MVC
  - RAPA
  - MVC+RAPA

- **CK (IU/L)**
  - Control
  - MVC
  - RAPA
  - MVC+RAPA

**Significance Levels**

- *******
- ****
Results (II)

- **Relative gene expression**
  - Caspase-3/GAPDH

- **Muscle myostatin (pg/mL)**
  - Control, MVC, RAPA, MVC+RAPA

- **Serum myostatin (pg/mL)**
  - Control, MVC, RAPA, MVC+RAPA

*Significant differences indicated by asterisks:*
- * indicates p < 0.05
- ** indicates p < 0.01
- *** indicates p < 0.001
Discussion & conclusions

• All the therapeutic interventions reduce myostatin levels, a negative regulator of muscle mass.

• Serum CK, a sensitive marker of muscle injury, was significantly lower in the MVC and RAPA groups.

• AST, a biochemical marker of muscular damage, was significantly lower in the MVC and RAPA groups.

• Caspase, a crucial mediator of apoptosis, was lower nearly in all the therapeutic groups, in particular the MVC group.

• All this data could support that MVC and RAPA preserves muscle quality in this model of frailty.

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