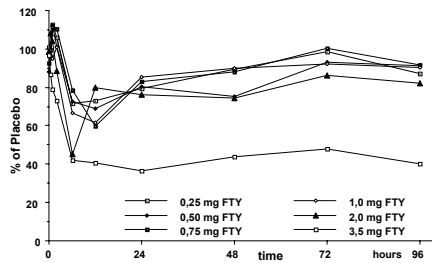


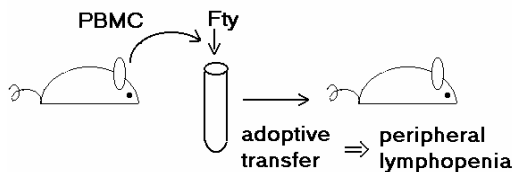
Background

- Prevents allograft rejection in synergism with CyA
- induces a reversible lymphopenia



Budde et al, J Am Soc Nephrol 13: 1073-83

- altered lymphocyte migration
- main target cells of Fty are lymphocytes



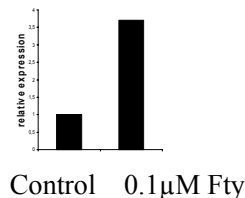
Methods

Signaltransduction analysis using Becton Dickinson Powerblot

- Human PBMC from a healthy volunteer were treated (n=3) with 0.1µM Fty720 for 12 h
- differential expression of 622 signal-transduction proteins were investigated
- we identified 10 proteins associated to cytoskeleton and cell adhesion

Results

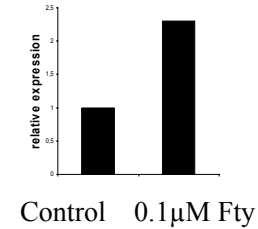
Fty increases 3.7±1.4-fold Rho expression



- Rho is an important regulator which orchestrates the reorganisation and formation of the actin cytoskeleton

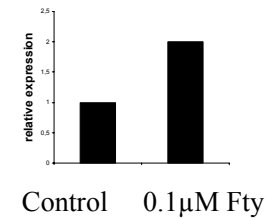
Fty increases 2.3±0.3-fold PTEN expression

- PTEN is a phosphatase
- PTEN interacts with PI3K/AKT signal transduction and cytoskeletal dynamics



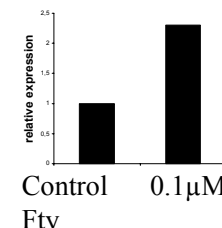
Fty increases 2.0±0.5-fold KAP3A expression

- KAP3A is an accessory protein for the microtubule translocator kinesin



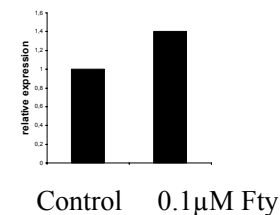
Fty increases 2.3±0.7-fold MAP 2B expression

- MAP 2B is involved in the assembly of microtubules



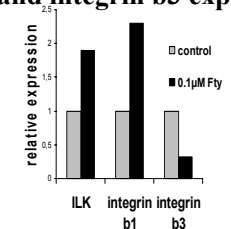
Fty increases 1.4±0.1-fold Moesin expression

- Moesin is an intracellular protein localized to the cytoskeleton
- Moesin modifies interaction of cytoskeletal and membrane proteins



Fty affects ILK, Integrin b1

and integrin b3 expression



- Integrin linked kinase (ILK +1.9±0.7) is localized to focal adhesion plaques and interacting with the cytoplasmic domain of integrin b1 and b3
- integrin b1 + 2.3±0.6
- integrin b3 - 3.1±0.4

Conclusions

- Using a proteomic approach, we identified putative mediators of the Fty signaltransduction pathway in human lymphocytes
- The identified proteins suggest that Fty interacts with cell adhesion and cytoskeleton organisation
- These features of Fty might play a role in Fty- altered lymphocyte mobility