

## L6 Immunosuppressants

### Calcineurin Inhibitors

**Cyclosporin** - calcineurin inhibitor

- need intermediate to produce their actions
- immunophilin + cyclosporin → cyclophilin

MoA of cyclophilin

- inhibits calcineurin's ability to dephosphorylate NFAT
- ↓ NFAT translocation into nucleus
- coz NFAT cannot enter nucleus if (P)
- ↓ gene transcription of IL2
- ↓ IL2 production
- weak proliferation signal
- ↓ clonal expansion & proliferation of T cell
- ↓ immune activity

SE : nephrotoxicity

**Sirolimus**

- aka Rapamycin
- produced by bacteria to prevent rejection
- x inhibit calcineurin activity
- inhibits mTOR (mammalian target of Rapamycin)
- inhibits IL2 signal transduction mechanism

SE : hyperlipidemia (↑ lipid levels)

<b>Cyclosporin / Tacrolimus</b>	<b>Sirolimus</b>
- inhibits calcineurin activity (via cyclophilin / FKBP immunophilin)	- inhibits mTOR
- ↓ NFAT into nucleus	
- ↓ IL2 production	- inhibits IL2 signal transduction mech

leads to ↓ clonal expansion of T cell

### Cyclosporin vs Tacrolimus vs Sirolimus

- cyclosporin : inhibits calcineurin via cyclophilin
- tacrolimus : inhibits calcineurin via FKBP (immunophilin)
- sirolimus : inhibits mTOR via FKBP

### Anti-metabolites

- cytotoxic drugs