UCSF School of Pharmacy

# *CYP3A5* genotypes and the impact of the phenotypes on tacrolimus levels in UCSF pediatric bone marrow transplant patients

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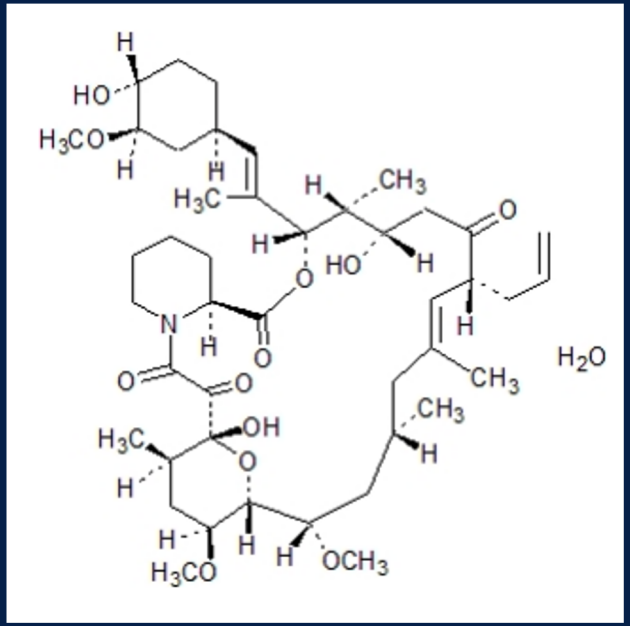
# Overview

- Background
  - Tacrolimus (TAC) in BMT (Bone marrow Transplant)
  - CYP3A5 polymorphisms
- Objective of the study
- Outcomes

# Tacrolimus

- Macrolide calcineurin inhibitor:
  - Variable pharmacokinetics
  - Narrow therapeutic window
  - CYP3A5 metabolism/polymorphisms
  - Weight-based dosing
- Bone marrow transplant:
  - Graft vs Host Disease (GvHD) prophylaxis
  - Trough goal at UCSF: 5-15 ng/mL



# CYP3A5 Polymorphisms

- Alleles of interest:
  - **1* = Functional allele
  - **3, *6, *7* = Non-functional alleles

# CYP3A5 polymorphisms impact tacrolimus' pharmacokinetics

- A meta-analysis that included 23 studies in different patient populations (renal and liver transplantation; 22 in adults, 1 in pediatrics):
  - CYP3A5-expressors (compared to non-expressors):
    - Require higher TAC doses to achieve therapeutic levels
    - Experience significantly higher acute rejection rates within the first four weeks of transplantation
    - OR: 3.27; 95% CI: 1.57–6.81

Tang H-L, Xie H-G, Yao Y, Hu Y-F. Lower tacrolimus daily dose requirements and acute rejection rates in the CYP3A5 nonexpressers than expressers: Pharmacogenetics and Genomics. 2011 Nov;21(11):713–20.

# Study Objectives

Identify the genetic and non-genetic factors associated with TAC concentration in pediatric BMT recipients.

Determine the effect on CYP3A5 phenotype on concentration of TAC in plasma when first pass metabolism is bypassed.

# Study Outcomes

**Primary Outcome:**

The effect of CYP3A5 phenotype on the concentration of TAC measured 24 hours after initial IV infusion.

**Secondary Outcome:**

The effect of CYP3A5 phenotype on time to achieving therapeutic TAC concentration.

# Thank you!