

**One Professor from Top 200 Universities in the World**

**Novel Biomarkers to Shorten TB Treatment**

Submitted by:

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**1st semester**

**M. Phil Pharmacology**

Submitted to:

**Dr. Hafiz Muhammad Irfan**

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**Advanced Chemotherapy**

Date of submission:

**June 28, 2020**

**College of Pharmacy**

**University of Sargodha**

**Rada Savic, PhD**

**Associate Professor**

Department of Bioengineering and Therapeutic Sciences

School of Pharmacy

University of California San Francisco, USA

**Biography**

Rada Savic is working as an Associate Professor at the School of Pharmacy in Department of Bioengineering and Therapeutic Sciences at the University of California San Francisco, where she leads her Global Health Data and Modeling Team. Dr. Savic is scientific leader on several Global Health large-data initiatives directed by Centers for Disease Control and Prevention (CDC), Bill & Melinda Gates Foundation, and World Health Organization. She trained in clinical pharmacology, biostatistics, pharmacy, and pharmacometrics at institutions in Sweden, France, Serbia, and US.

Her research work employs computational systems to study the dynamic interplay between disease progression, drug and its response across related scales (molecule, cell, tissue, organ and whole body) in order to determine contributory links underlying variability in (safety and efficacy) clinical outcomes. By integrating multi-scale, and multi-level clinical data, she is working to establish the right dose, right schedule and right treatment duration of various therapies, potentially generating novel, precise and tailored treatment preferences to patients with unmet need more rapidly.

**Research expertise**

Infectious diseases: (tuberculosis, malaria, HIV and pediatric infectious diseases), Oncology, Diabetes, Pharmacometrics, Clinical pharmacology, Pharmacogenetics, Developmental pharmacology, Disease progression models, Drug development, NONMEM, Modeling and Simulations, Clinical Trial Designing.

**Educational Profile**

PhD Pharmacometrics Uppsala University, Uppsala, Sweden, 2008

MS Biomedical Sciences Uppsala University, Uppsala, Sweden, 2004

BSc Pharmacy University of Belgrade, Serbia, 2003

**Research Activities**

**Savic Lab**

Integrative Pharmacology Laboratory

1. **Clinical and Translational Tuberculosis**

The Savic Lab aims to develop translational platforms able to predict drug exposure levels and efficacy in clinical studies and, thereby, to optimize dosing. The lab is making progress toward shifting the focus of the clinical development of new tuberculosis drugs from basic safety and efficacy to specific safety endpoints that will reduce the amounts of trials, subjects, and time necessary for drug approval. This will enable new safe and efficacious therapies to be brought to market more quickly and with more efficiency and will prevent unnecessary deaths due to drug resistance and treatment failure.

* Clinical TB:Model-Based Analysis of Tuberculosis Biomarkers
* Clinical TB:Nonlinear Mixed-Effects Modeling of Rifapentine PK and PD
* Systems Model of TB Including Translation from EBA Study to Clinical Trial Efficacy
* Phase-IIA Early Bactericidal Activity (EBA) Studies
* Modeling Pyrazinamide Lesion-Specific Pharmacokinetics and Efficacy from Rabbit Data
* TBI-223 Model for Human Translation
* Optimizing Clofazimine (CFZ) for TB in Children
* Translational Baseline Model

1. **Pediatric Infectious Diseases and Malaria**

The Savic Lab is working to optimize anti-infective treatment and prevention strategies for vulnerable populations. Our goals are to improve understanding of the unique treatment needs of children – especially those made vulnerable due to HIV and malnutrition – in order to eliminate preventable deaths due to infectious diseases in resource-limited settings and to recommend evidence-based policy changes to anti- infective indications, choices, and dosing regimens for vulnerable populations.

* Pharmacokinetic/Pharmacodynamic Research for Optimal Dosing Regimens for Children

1. **HIV Prevention**

The Savic Lab’s goal is to optimize the prevention of HIV infection through PK/PD modeling and simulation. To accomplish this, we are working to identify and reach those most vulnerable and at risk of HIV infection, and identify optimal treatment and formulation options through considering alternative target drug concentrations and individual commitment to adherence in order to establish a quantitative relationship between tenofovir levels and HIV prevention.

* Mechanistic Assessment of HIV Growth in Tissue Explant Samples
* Individual Level Data Meta-Analysis from Pre-Exposure Prophylaxis (PrEP) Clinical Trials

**Global Research Projects**

**Active Projects**

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| --- | --- | --- | --- | --- | --- |
| Project | Sponsor | Location(s) | Topics | Start | End |
| *Adherence Monitoring impact in Global Health - Planning Grant* | Bill & Melinda Gates Foundation | Uganda | Tuberculosis, Treatment Adherence | 11/1/19 | 4/30/20 |
| *Impact of Pregnancy on Tuberculosis* | Rutgers University | Uganda | Tuberculosis, Pharmacology and Drug Treatment, Women's Health, Labor and Delivery, Newborn and Infant Health | 11/1/18 | 7/31/20 |
| *Novel Biomarkers to Shorten TB Treatment* | Rutgers University | United States | Tuberculosis | 7/22/16 | 5/31/21 |
| *Lesion Drug Penetration and Translational Modeling* | Bill & Melinda Gates Foundation | United States | Tuberculosis, Drug and Diagnostics Development | 10/28/19 | 9/30/21 |
| *Identifying Optimal Treatment Strategies for Tuberculosis Treatment* | NIH National Institute of Allergy and Infectious Disease | Kenya;  Malawi;  Uganda;  Zimbabwe; S. Africa; China; India; Vietnam; Thailand; Brazil;  Peru; Haiti | Tuberculosis, Pharmacology and Drug Treatment | 1/16/19 | 12/31/23 |

**Recent Publications**

* Hibma JE, Radtke KK, Dorman SE, Jindani A, Dooley KE, Weiner M, McIlleron HM, Savic RM. Rifapentine Population Pharmacokinetics and Dosing Recommendations for Latent Tuberculosis Infection. Am J Respir Crit Care Med. 2020 May 15. PMID: 32412342.
* Garcia-Cremades M, Solans BP, Hughes E, Ernest JP, Wallender E, Savic RM. Response to "Quantitative clinical pharmacology input to SARS-CoV-2 therapeutics should be based on robust data". Clin Pharmacol Ther. 2020 Apr 29. PMID: 32348544.
* Walsh KF, McAulay K, Lee MH, Vilbrun SC, Mathurin L, Jean Francois D, Zimmerman M, Kaya F, Zhang N, Saito K, Ocheretina O, Savic R, Dartois V, Johnson WD, Pape JW, Nathan C, Fitzgerald DW. Early Bactericidal Activity Trial of Nitazoxanide for Pulmonary Tuberculosis. Antimicrob Agents Chemother. 2020 Apr 21; 64(5). PMID: 32071052.
* ee SA, Telwatte S, Hatano H, Kashuba ADM, Cottrell ML, Hoh R, Liegler TJ, Stephenson S, Somsouk M, Hunt PW, Deeks SG, Yukl S, Savic RM. Antiretroviral Therapy Concentrations Differ in Gut vs. Lymph Node Tissues and Are Associated With HIV Viral Transcription by a Novel RT-ddPCR Assay. J Acquir Immune Defic Syndr. 2020 Apr 15; 83(5):530-537. PMID: 32168200.
* Garcia-Cremades M, Solans BP, Hughes E, Ernest JP, Wallender E, Aweeka F, Luetkemeyer A, Savic RM. Optimizing hydroxychloroquine dosing for patients with COVID-19: An integrative modeling approach for effective drug repurposing. Clin Pharmacol Ther. 2020 Apr 14. PMID: 32285930.