Department of Biochemistry
Yong Loo Lin School of Medicine

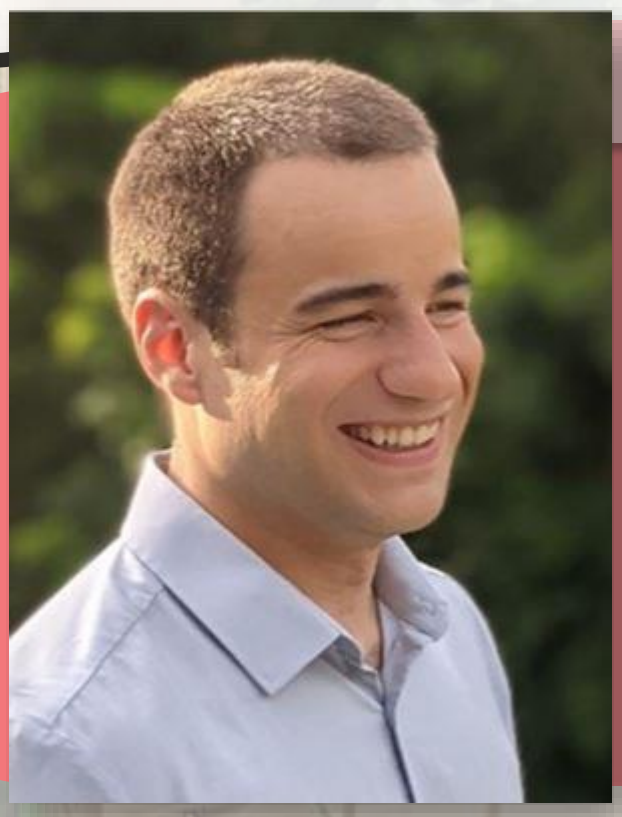
PhD Oral Defense (Virtual)

EXTENDING HEALTHY LIFESPAN BY SYSTEMATICALLY TARGETING AGING PATHWAYS SYNERGIES

Aging is the main risk factor underlying the dramatic increase in incidence of cancer, cardiovascular and neurodegenerative diseases in aging populations. However, evidence over the last three decades has revealed that aging rate and individual aging-trajectory is more than previously appreciated. This fact opens the possibility for therapeutically relevant pharmaceutical interventions to ameliorate the impact of population aging in terms of disease burden and to potentially even delay the aging process itself.

Recent insights from work on drugs and genes affecting lifespan in model organisms has revealed that the most significant lifespan-effects are the result of pathway synergy and drug-drug interactions. While exciting, it is currently unclear how common such synergistic interactions are or how to best leverage them therapeutically. There is currently no validated approach to construct such interactions rationally and systematic screening for such interactions is challenging due to the combinatorial explosion in search space.

I have created and validated an automated high-throughput screening platform for the identification of healthspan-extending drugs in Caenorhabditis elegans. Using this system, conducted a large pilot screen for combinatorial drug benefits, identifying several new drug pairs with additive or synergistic benefits in terms of healthspan and lifespan. Furthermore, I generated and analysed transcriptional signatures (RNA-Seq) for each drug in my dataset of lifespan-extending drugs. This transcriptomics information, coupled with the results of the screen, were then used to test the nature of drug synergies and explore potential approaches to predict beneficial drug-drug interactions based on transcriptional data of individual drugs. This analysis can be used to identify potentially synergistic drug combinations.



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Date/Day: **22 September 2021, Wednesday**
Time: **10am**

Seminar Platform: **Zoom**
Link: Click here
Meeting ID: 886 2416 4228
Passcode: 583776

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