

*Open Problem Set: igKnight Scholarship*¹

igKnight Founding Members

February 16, 2016

¹ Mail: hello@igknight.zendesk.com

This document describes six open problems within the scope of igKnight. The participants are encouraged to read through all six, pick a problem to focus on and begin their journey in the program. These problems are picked from three particular areas in life sciences: Molecular biology, Clinical applications and Behavioural sciences. The problems provided not only explore the field, but also encourage the participants to understand the broader context such as the socio-economic impact on the health-care system.

The organization of this problem set is explained as follows. The problems are organized as topics here and within each topic is a short description of the main focus of the problem. Additionally, there are several support questions to help the participant think about what to keep in mind while reading the research literature. These support questions are only meant as mental checkpoints to guide inquiry, not necessarily strict questions to be answered. Finally, to support the scholars entering the competition, office hours and seminars will be provided as an opportunity to clarify any of the topics and ask questions.

Topic 1: Immunotherapies and Stroke

A recent review by Fu et al. discusses the use of immunotherapies such as those used for multiple sclerosis or new anti-inflammatory drugs for the treatment of acute stroke and decreasing the collateral side-effects such as permanent tissue damage in the brain.

Questions

- Describe this apparent connection between the use of immunotherapy drugs or anti-inflammatory drugs for stroke
- What is the role of the immune modulators and more broadly the immune system in interventions for stroke?
- What is the social impact of having MS or an acute stroke? What public health policies accommodate the patients going through these circumstances back into their workplace?
- How prevalent are degenerative diseases? Are there any preventive measures or programs for improving the health of those susceptible to some type of brain degeneration? ² What do the results

² A few startups are tackling mental health and particular rehabilitation by incorporating technology, find a few of them and describe how they work, what the success is like and if they have any published any studies

from those programs look like? (Or put differently, what does the data say?) Are they successful in any extent so far?

- What possible therapeutic targets are being examined from this connection between immunotherapies and stroke? Any recent data from repurposing drugs? What does the success rate look like in animal models?
- Gathering from other Opinions or Perspective papers, what does the future of this connection look like?

Topic 2: Drug discovery and Stem-cell treatments

The translation of bench-research to therapeutic targets is one of the most crucial steps in clinical research. Unfortunately, it is also the most expensive one. A recent article in the New York Times ³ estimates that the drug discovery process and the cost of a new drug going through the entire pipeline may be around 2 billion. Stem cells may be changing this game, let's figure out how.

Drug discovery

- What is a drug discovery pipeline?
- What costs does a drug candidate incur while going through the initial phases of discovery and validation?
- Discuss the entire approval process. Start from a drug candidate in a lab, such as viparol and describe its progression from gathering animal data, to applying for FDA approval and then all the phases of the approval process.
- In the future, games and mobile apps may get FDA approval (some apps already have it) ⁴. What social or peer pressure elements can change behaviours? How are these life-style changes impacting the lives of chronic patients?

Stem cell treatments

- What are the advantages and improvements over traditional approaches?
- What are the major therapeutic targets for stem cell treatments?
- What is the current state of stem cell treatments that have been translated to clinical trials? Which trials have been completed? And what does that data yield?
- How can more stem-cell treatments be incorporated into the clinic? Why are there high barriers to entry for stem-cell treatments from academic labs to clinical trials?

Topic 3: Memory and Stress

College students are always stressed. And at the same time, we have to memorize copious amounts of information to stay on top of our classes. In this topic, we will study how the connection between how information gets encoded in the brain and how stress influences it. Additionally, the current models for representation of memory need to be updated based on recent discoveries. Let's figure out what these new changes are.

Memory encoding

- What are engrams? How is memory encoded in engrams? What are representational cues in the context of engrams?
- How has representations of memory and the models that describe memory changed over time? Why do we need improvements on classical theories such as the Cable theory?
- How do we form selective memories? What is guided search? How does attention develop?

Stress and the brain

- How has the context of brain health evolved over the years?
- How does stress relate to synaptic plasticity? More broadly how does stress impact working memory and short-term memory?
- How does stress influence the physiological mechanisms behind our social lives?

Topic 4: Psychiatric disorders and Pain

In recent studies, several voltage gated channels have been linked to modulate pain, especially with migraine. As more data is becoming available, the connection between disorders of voltage-gated channels and pain is becoming increasingly clear. We examine this connection here and in particular, how dysregulation of voltage gated channels can cause psychiatric disorders.

Voltage gated channels

- What are the different types of voltage gated channels that exist? What's the purpose of having voltage gated channels? How do they get activated, deactivated and inactivated?
- How do voltage gated channels act in the CNS and PNS to modulate pain?

- Which channels have generated potential clinical targets? Which of those targets are undergoing translational research? Which therapeutic targets have successful drugs developed for them? What's the data on the success rate of those drugs? What new clinical trials are ongoing targeting voltage channels?

Pain and Psychiatric disorders

- What is the connection between migraine and voltage gated channels?
- What is the socioeconomic impact of migraines? More broadly, what about headaches? How do they influence the social lives of the patients suffering from chronic headaches?
- What drugs are most commonly used in migraines? What are the latest drugs approved in the area and what is their mechanism of action?
- What roles do calcium channels play in neurological and psychological diseases?

Topic 5: Toxicity and Metabolic homeostasis

The liver filters the blood and the blood becomes detoxified in the process. This process is incredibly effective but not all toxins get removed, one exception to this process is the drugs that we intake. They may get broken down into side-products but those products can have some harmful effects. Chronic treatments often have associated long-term risks that are not very well understood. Chemotherapy is one such treatment that we study in this topic.

Toxicity

- How does a systems approach help in studying toxicity produced through chemotherapy?
- What is the mechanism of cardiotoxicity induced by the chemodrugs?

Metabolic homeostasis

- What physiological changes occur during starvation? How can autophagy assist in breaking down varied sources of energy?
- What is the persistence pathway? What is the alarmone ppGpp and what is its mechanism of action?
- How can a systems approach be applied to study the persistence response and metabolic homeostasis?

Topic 6: Hypertension and Myopathies

The lifestyles and work-choices in western society have led to ever increasing epidemic of hypertension. Often called the silent-killer, hypertension has very detrimental long-term effects that have been very well studied. We know that many lifestyle changes can decrease the risk factors that cause myopathies. In this topic, we focus on the cardio-renal system and its eventual dysfunction.

Cardiac output

- Describe the process of an acute heart failure? What is the socio-economic impact of heart failures? What factor does the obesity epidemic play in heart failure? What other health factors are involved in myocardial infarctures?
- Why is hypertension called the silent killer? Describe the cardiac-renal relationship. How do cardiac dysfunction relate to renal failure?
- What role to mast cells play in myopathies? How are mast cells being used as a therapeutic targets? What current trials are ongoing? What does the success rate looks like? What successful candidates have been produced? Any current candidates in Phase III?
- What is viral myocarditis? What is the mechanism of action for the virus? How does it spread to the valves? What therapies are available? What are the possible treatment options?