**Research Theme** (Please indicate as appropriate)

- ☒ Metabolic Disorders
- ☐ Dermatology & Skin Biology
- ☐ Health Systems & Population Health
- ☐ Family Medicine & Primary Care
- ☐ Infection & Immunity
- ☐ Neuroscience & Mental Health
- ☐ Medical Education
- ☐ Others (Please specify):

**Research Project Title:**
Immunopathogenesis of Nonalcoholic steatohepatitis (NASH)

**Project Description:**

**The Next Big Epidemic.** Nonalcoholic steatohepatitis (NASH) is a significant cause of chronic liver disease and the most severe form of nonalcoholic fatty liver disease (NAFLD). NASH can progress to life-threatening liver diseases that burden public health as well as the health care system. The worldwide prevalence of NAFLD was ~25% and the proportion of NAFLD patients with NASH is about 10-30%. NASH is highly prevalent in populations suffering from obesity and from type 2 diabetes. This increasing obesity and diabetes trends portend that NAFLD and NASH will increase dramatically over the next few decades. Furthermore, NASH may serve as a surrogate marker for extrahepatic complications including cardiovascular disease and cognitive deficit.

NASH is underdiagnosed and undertreated. The current standard of care for NASH is weight loss through diet and exercise, which is a clinically challenging goal to achieve. There are no licensed therapies for NASH. NASH is a chronic yet silent disease, which means that most patients are unaware of their liver conditions. There is currently no effective treatment for NASH, due in part to a poor understanding of its immunopathogenesis.

**Hypothesis:** Metabolic and immunological changes that occur during disease progression will yield novel biomarkers and therapeutic targets for NASH/NAFLD.

**Aim:** Unravel the dynamic immune landscape in the liver during NASH development.

**Brief summary of main Methodologies and/or Techniques to be learned during the proposed PhD (experimental or analytical):**

**Animal model:** Using a novel mouse model that combines a proprietary all-natural high-fat diet with a thermoneutral environment to induce the full sequelae of NAFLD and NASH in a shorter time frame. This model closely mirrors human NAFLD to NASH transition.

**Cell biology:** Histology, immunohistochemistry, single cell preparation, FACS sorting, bone marrow transplantation.

**Molecular biology:** RNA-seq; ChIP-Seq, and data analysis. Meta-analysis from public database.
Keywords: Nonalcoholic steatohepatitis, Animal model, Data Analysis.
## Supervisor(s)

### Primary Supervisor

<table>
<thead>
<tr>
<th>Name of Supervisor:</th>
<th>Andrew Tan Nguan Soon</th>
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</thead>
<tbody>
<tr>
<td>Designation:</td>
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### Co-Supervisor *(need not be determined at this time)*

<table>
<thead>
<tr>
<th>Name of Supervisor:</th>
<th>Walter Wahli</th>
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</table>

## Main Location of Research Work *(Please indicate as appropriate)*

- [ ] LKCMedicine Experimental Medicine Building @ Yunnan Campus
- [x] LKCMedicine Clinical Sciences Building @ Novena Campus

## Other Information

1. Does the proposal need IRB’s approval?  
   - [ ] Yes  
   - [x] No

   If “Yes”, is the IRB’s approval in place?  
   - [ ] Yes  
   - [ ] No

2. Does the project involve contact with patients?  
   - [ ] Yes  
   - [x] No

3. Is there a potential for overseas academic exchange as part of this research project?  
   - [ ] Yes  
   - [x] No

   If “Yes”, please specify:  
   

   _______________________________________________________

   _______________________________________________________