## Propositions associated with the thesis

## The State of STATs in Primary Immunodeficiencies:

## Molecular Diversity and Implications for Therapy

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- 1. Increased STAT1 phosphorylation observed in cells with gain-of-function variants in the SH2 domain of STAT1 is not resulted from impairment of STAT1 dephosphorylation as observed in variants located in the coiled-coil domain or in the DNA-binding domain of STAT1.

  This thesis
- 2. Elaborative biological investigations for the disease pathogenesis could provide clues for precision targeted therapeutic strategies.

  This thesis
- 3. Baricitinib may has a promising therapeutic efficacy in patients with *STAT1* GOF variants as well as in patients with interferonopathy.

  This thesis
- 4. In blood cells from patients with *STAT3* GOF variants, STAT3 phosphorylation is rarely affected. Cellular GOF phenotypes of *STAT3* activating variants was demonstrated by enhanced intrinsic STAT3 transcriptional activity. Therefore, STAT3 phosphorylation is not the recommended test for the diagnosis of STAT3 GOF phenotypes. *This thesis*
- 5. The human system harbors seven STAT subtype molecules, dysfunction of only one STAT may disturb the equilibrium of the multi-STAT system. Keeping the balance is therefore indispensable for the healthy state of STATs.

  This thesis
- 6. Early recognition and diagnosis of primary immunodeficiency disorders is important for patient prognosis and quality of life.

  Jordan S. Orange. Frontiers in Medicine, 2016
- 7. The Clinical Immunology Society supports the use of genetic testing by clinical immunologists to provide a "state of the art" diagnosis and precision treatment for primary immunodeficiency patients. *Jennifer R. Heimall. Journal of Clinical Immunology*, 2018
- 8. CRISPR systems are being robustly adapted to improve the efficacy of immunotherapies by enhancing their potency, mitigating toxicity, reducing manufacturing costs and facilitating the discovery and development of new immunotherapeutic strategies.

  Hao Yin. Nature Reviews Clinical Oncology, 2019
- 9. Translational medicine professionals must be creative, a skill which is difficult to teach and measure. This creativity is fundamental to driving new concepts in the design and practice of trials as well as of medical products and the translational medicine pathway itself. Translational medicine professionals must also use their creativity to develop collaborations with research centers, universities and commercial centers.
  - Faekah Gohar. Frontiers in Medicine, 2018
- 10. Progress is made by trial and failure; the failures are generally a hundred times more numerous than the successes; yet they are usually left unchronicled.

  William Ramsay. Harper's Magazine, 1904
- 11. Intelligence is the ability to adapt to change. *Stephen Hawking, Physicist*