PROPOSITIONS

TO THE THESIS

Helicobacter pylori and Gastric Cancer: From Tumor microenvironment to Immunotherapy

By

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1. Ptc-dependent Smo-independent non-canonical Hedgehog signaling increases Wnt/Notch providing an obvious explanation for the failure of Smo antagonists in combating gastrointestinal cancer. *(this thesis)*

2. Hedgehog-targeted therapy in GI cancer should be directed at inhibiting Hedgehog-Ptc interaction and not at Smoothened. *(this thesis)*

3. The strength of agreement between endoscopic and histological gastric atrophy was moderate and showed substantial geographical discrepancy. *(this thesis)*

4. Relying solely on endoscopic screening for atrophic gastritis requires local validation. *(this thesis)*

5. Checkpoint inhibitor therapy in general, and PD-1-directed therapy in particular, constitutes a rational therapeutic avenue for advanced gastric cancer. *(this thesis)*

6. High prevalence of infection with *H. pylori* strains is associated with known virulence genotypes but also with high genetic diversity. This highlights the importance of identifying gene variants for early detection of virulent genotypes. *(this thesis)*

7. Rac/Rho signaling emerges as the pathway targeted by microgravity to inhibit immunity in space travel, implying that stimulation of this pathway might be beneficial in gastric cancer.

8. The ongoing revolution in cancer therapy will ultimately result in immunotherapy becoming prioritized over classical chemo-or radiotherapy-based therapies.

9. We Need Better Insights, Not More Data (Danny Brown). This notion corresponds to the observation that big data efforts have not yielded improved prognosis for gastrointestinal cancer patients.

10. Seriousness is the only refuge of the shallow (Oscar Wilde). This notion corresponds with my observation that the Nobel prize winner Andre Konstantinovich Geim discovered graphene while playing with cellotape.

11. A smooth sea never made a skilled sailor (Franklin D. Roosevelt)