Module 7 Assignment

585.751.81 Immunoengineering

1. Here are some examples of recent start-ups tackling challenges related to infectious diseases, and pick one and research further: (15 points)
   - Karius
   - Moderna
   - Day Zero Diagnostics
   - VIR Biotechnology
   - IDbyDNA
   - Vaxess
   - You may also choose a start-up not found on this list that you find interesting

VIR Biotechnology

As you research, answer briefly (1-2 sentences for each):

1. What does their technology do and what disease is targeted?

VIR Biotechnology has built a monoclonal antibody (mAB) discovery platform and a T Cell-Based Viral platform enabling to target a range of infectious diseases such as Chronic Hepatitis Delta (CHD), Hepatitis B (CHB), HIV, respiratory syncytial virus (RSV), Influenza, COVID 19 and pre-cancerous human papillomavirus (HPV) lesions.

2. What problem does their technology solve?

VIR Technology leverages the human immune system to fight viruses, employing machine learning and artificial intelligence, to engineer effective medicine from human-derived antibodies.

3. What stage of development are they at?

The FDA has granted approval for the COVID 19 medicine, while the remainder of the drug pipeline is either in preclinical or Phase 2 clinical trials.

2. A new diagnostic test is being developed for tuberculosis. Tests with characterized patient samples have been performed on the new test. Values below correspond to the number of samples in the test positive for tuberculosis. (10 points)
   - Calculate the sensitivity and specificity of the test for each group and also for all groups combined.
   - Also, comment on the utility of this test based on these criteria.

HIV– groups (n = 222)
TB+ = 50/54
Latent TB = 8/62
Nontuberculosis mycobacteria = 6/64
Healthy controls = 0/42

	TB+, Latent TB	NonTb + Healthy
Positive Test Result	58	6
Negative Test Result	58	100
	116	106

Sensitivity	0.5
Specificity	0.943396226

For people without HIV, the test has a 50% probability of correctly detecting TB in those who have it, this means that for people without HIV who have TB, the test performs no better than random chance. However, within the same group, the test shows a very high probability, ~ 94% of correctly identifying individuals without TB as healthy. For individuals without HIV who do not have TB, the test is very accurate classifying them as TB-free.

HIV+ groups (n = 180)
Pulmonary TB+ = 70/80
Extrapulmonary TB+ = 36/42
TB- = 6/58

	TB+, Extra.TB+	TB-
Positive Test Result	106	52
Negative Test Result	16	6
	122	58

Sensitivity	0.868852459
Specificity	0.103448276

In the group of people with HIV, the test performs differently; It can significantly detect people with TB, achieving an accuracy of approximately 86%, which means that for people with HIV who have TB, the test effectively detects the infection in most cases. However, the test performs poorly for healthy individuals within the same group. It struggles to accurately classify healthy people as disease-free.

HIV- + HIV+

	TB+	TB-
Positive Test Result	164	58
Negative Test Result	74	106
	238	164

Sensitivity	0.68907563
Specificity	0.646341463

Assuming that the experiment is representative of the number of people with HIV and without, including both healthy individuals and those with TB, the test's overall ability to distinguish between TB+ and TB- individuals is subpar. Specifically, the test ability in detecting TB+ individuals and correctly identifying TB- people are approx. 68% and 64%. These performances could put on pause the approval for the test's deployment.

3. Compare and contrast *Large scale screening* to *Mechanistic insight* approaches to discover new therapeutic targets. Please focus on the advantages and disadvantages of each approach. (15 points)

	Advantages	**Disadvantages**
Large scale screening	• High throughput: due to automation allows the rapid screening of very large libraries of compounds against a specific target and can accelerate the identification of potential active compounds or hits. • Does not require prior knowledge for finding a novel drug.	• Initial set up costs of HTS technology could be significant. • May not be as specific as other technics (false positives/negatives). • May require the libraries to be established which could be time consuming and costly. • With an increase of throughput: loss of the physiological relevance, and impact on host toxicity. • Provides limited insights into the mechanistic action of the compounds.
Mechanistic insight	• Provides detailed insights into the molecular mechanisms and pathways through which compounds exert their effects. • Insights of mechanism of actions can help in	• Low throughput: compared to HTS, analyze of fewer compounds or hypotheses at a time • Requires understanding of the disease. • Require more resources, time and potentially more sophisticated

		predicting and understanding drug resistance, adverse effects and could reduce the failures rates in later stages of drug development. • Allows rational design and can lead to a more targeted and potentially more effective therapy. • Enable to answer theoretical and fundamental questions with simulation.	tools and models from researchers. • Compared to other methods has a higher chance of failure.

4. Compare and contrast the four major different types of biologic therapeutic approaches. In your analysis answer: (20 points)
   • When would you want to use each approach for infectious disease?
   • What is one of the major advantages and disadvantages to each approach?
   • What design criteria are shared between approaches in creating a therapy?

5. Design a biomaterial therapeutic to treat one of the following infectious diseases:
   • Tuberculosis (Bacteria)
   • Malaria (Parasite)
   • HIV (Virus)

   In your consideration of your design, please list specifically how the therapeutic was designed with design constraints such as:
   1. Manufacturing/Cost
   2. Safety
   3. Specificity
   4. Potency
   5. Biomaterial properties – e.g. stiffness, degradability, size, shape, etc.