FRAAI exam
Immunology part

1. Why are $CD4^+$ T-cells so important in the immune response? Describe the heterogeneity within this T-cell population and its importance in understanding basic mechanisms underlying immune-mediated diseases. What Th-cell subpopulations are critically involved in allergic diseases. *(10 credits)*

Answer: critical role of Th cells in maturation of B-cells to produce antibodies en CD8+ cytotoxic cells to mature into tumor- or virus-specific killer T-cells. They do this by the release of cytokines and cell-cell interactions. Subpopulations: Th1 (chronic inflammatory auto-immune diseases and transplant rejection), Th2 (allergy, (no disease: pregnancy), Treg (controlling all other T-cell populations, tolerance induction) and Th17 (early tissue defense against infections) populations. In allergy: mainly Th2 and Tregs (IL-10).

2. What are the essential differences in the immune response to allergens between the allergic sensitization phase and the allergen exposure phase? What therapeutic strategies are used based on this knowledge to treat allergic individuals? What potential new type of drug would you develop based on this knowledge and which is not on the market yet? *(10 credits)*

Answer: sensitization: Th2 and IgE formation in response to repeated low dose exposure to allergens on a mucosal surface which can load (sensitize) mast cells. Allergy: crosslinking of these bound IgE molecules on mast cell surface by the new exposure to allergens and subsequent histamine release which is responsible for the typical type I allergy symptoms. Therapies: anti-histamines or mast cell membrane stabilizers (no effect of histamine and blocking of symptoms), corticosteroids (block cytokine release and thus Th2 formation and IgE production), immunotherapy (restore the altered Th1-Th2 balance and induction of Treg by injection of rapidly increasing doses of allergens in seasonal allergies). Disadvantage of all of these strategies is the modification of Th cells and thereby interfering with the normal functions of these cells (protection against extracellular and intracellular infections) New drug: anti-IgE preventing binding of IgE molecules to mast cell (and basophil) high affinity IgE receptors (advantage no interference with Th cells and no side effects).

3. What unique properties of IgE antibodies compared to other antibody isotypes make them the hallmark of allergic disease? Describe the working mechanism underlying the therapeutic use of anti-IgE antibodies in patients with allergic diseases. *(10 credits)*

Answer: IgE is rigid and well suited to bind to antigens that contain repeating allergenic epitopes and IgE can bind to high affinity IgE receptors expressed on mast cells (mucosal tissues and skin) and basophils (blood). Anti-IgE: see answer to questions 3.

Food Chemistry part

1. To test a vegetable protein hydrolysate for the presence of a Kiwi allergen, samples have been tested with a specific anti-Act c1 antibody. Your standard is a solution of pure Act c1 protein. (i) Explain how you could use a competitive ELISA for this purpose; (ii) Discuss if using a specific anti-Act c1 antibody and an anti-total-Kiwi protein antibody would give the same results. If the results differ, motivate which

antibody gives the more relevant results. (iii) How can you calibrate a competitive ELISA? *(10 credits)*

Answer:

2. Imagine you are a company's quality manager and you receive two messages from the consumer desk. Message one describes a whole family complaining about stomach cramps and nausea. They related this to a meal they had a day before, possible containing one of your products. Message two describes a complaint of a girl who felt sick just 30 minutes after having had a candy bar made by your company. (i) Interpret each of these messages according to the adverse reactions classification scheme. (II) describe and motivate the actions you would recommend to take in each of the two cases. *(10 credits)*