COMBATTING EMERGING BIOLOGICAL THREATS – PREPARING FOR THE FUTURE TODAY

Harnessing The Power Of Cell Assembly Programmed (cap) Organs: All Organs Samples Available For Threat Assessment And Regeneration As A Countermeasure

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Current organoid technology has been a bright spot for investigating the pathogenesis of diseases, developing screening assays for new drugs, and forecasting toxicity, but improvements will amplify its power. We have championed our version of organoids formed by combining epithelial/mesenchyme cells together rather than using a single cell type, and piling cells on an even surfaced membrane rather than creating balls of cells. Conceptually, our data indicate that human cells retain their ability to form the complex structures seen in the micro-physiology of the correct placement of cells into tissue sheets and creation of organ components composed of different cell types. This refutes the notion that cells only arrange into organ structures during development and lose that ability in adulthood. The use of inkjet printing technology was initially offered as a way to control the placement of cells to recreate the micro-physiologic arrangements seen in organs. Placing cellular building blocks in order is not appropriate here because cells are constantly migrating and will rearrange themselves within a day even when stacked neatly by an inkjet printer. Our data indicate that cells are running programs to determine what steps they need to take in order to be useful to the collective organism. One program type is cellular differentiation, where cells receive information from surrounding cells on what type of cell is needed in their particular niche. Stem cells are useful because they have a clean slate, where they are highly flexible in becoming any cell type needed. Several research groups have identified treatments that can be used in the lab to trigger stem cells to form a certain lineage, but we worked on a second program running that determines the spatial arrangement of the cells. We found that a timed series of treatments aimed largely at signaling pathways can be used in the lab to trigger differentiating cells to migrate into correct positions to form arrangements of cells needed to achieve basic organ function, discovering cell assembly programming (CAP). Our early efforts led to our publication on 'cell sorting' and an issued US patent on forming full-thickness human skin. Now, using our programming steps, we are able to form both hair follicles and sweat glands, a highly useful step to offering injured warfighters fully functional lab replacement skin. Recently, an academic researcher used our cell sorting technique and saw hair follicles too, but without CAP had to wait at least 10 weeks to see hairs growing into an organoid ball. With CAP such structures form within 1 week. Using CAP with stem cells creates many different organ types, we show lung alveoli and bone osteon. Creating samples of all the organs will empower quality data for all the applications foreseen for organoids. Most significantly, CAP cells can be implanted directly into mice and give rise to human skin (our JID Cell Sorting paper), indicating that direct implantation of CAP cells at locations of organ damage is useful in regenerating organs, providing the ultimate long-term Medical Countermeasure for the injured warfighter.

The ideas presented were developed at HOF Therapeutics where future work will be conducted.