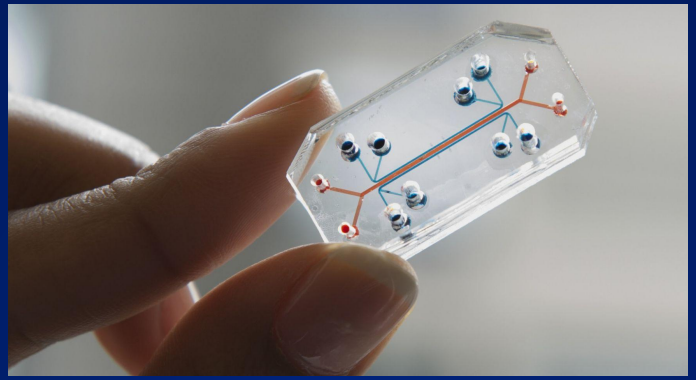


Gut-On-A-Chip to Test for Food Allergies and Intolerances

Annika, Melissa, Nadeen, Taylor

Background

- 32 million people in the US suffer from food allergies
- Food allergies cause immune system dysfunction and painful digestion
- Many people with food allergies try elimination diets
- Lots of failure due to timeliness and difficulty

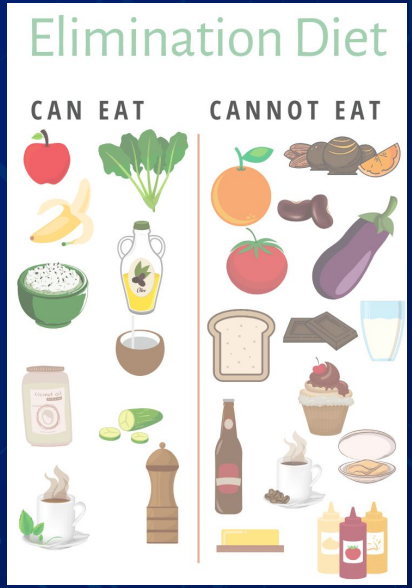
Current Gaps

Food Sensitivity Tests

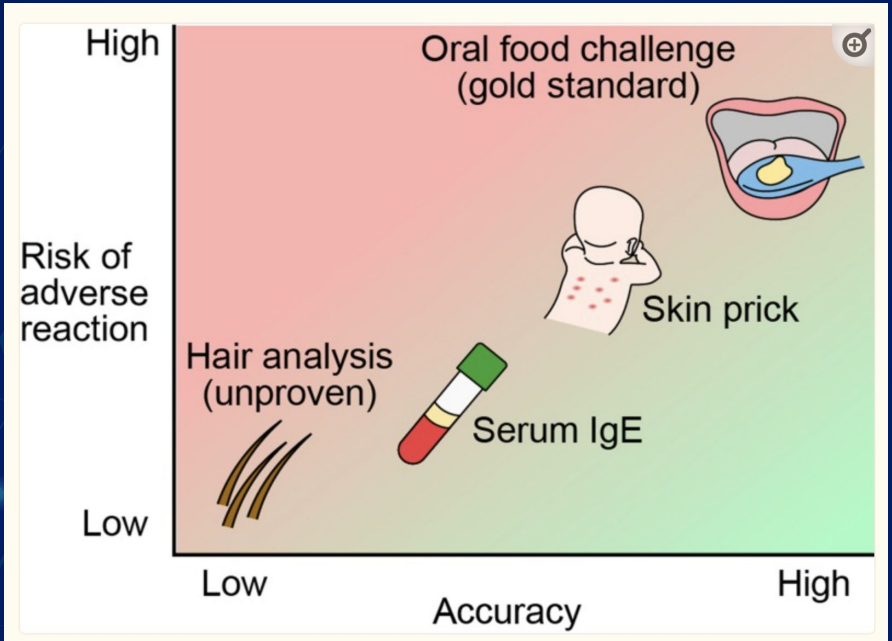
1. Blood work required
2. Does not give good insight into overall digestive dysfunction

Elimination Diets

1. Time-consuming
2. Difficult to follow through with



Current common allergy testing methods present a trade off between accuracy and risk of adverse reactions.



Castaño, Nicolas, et al. “Microfluidic Methods for Precision Diagnostics in Food Allergy.” Biomicrofluidics, vol. 14, no. 2, Apr. 2020, p. 021503. PubMed Central, https://doi.org/10.1063/1.5144135.

Key Features of the Gut

Transport

Absorb and transport nutrients from digestion to vasculature

Specialized Cells

Microbiomes to make vitamins and break down complex foods

Immunity

Trains the immune system and rids system of pathogens

Structural

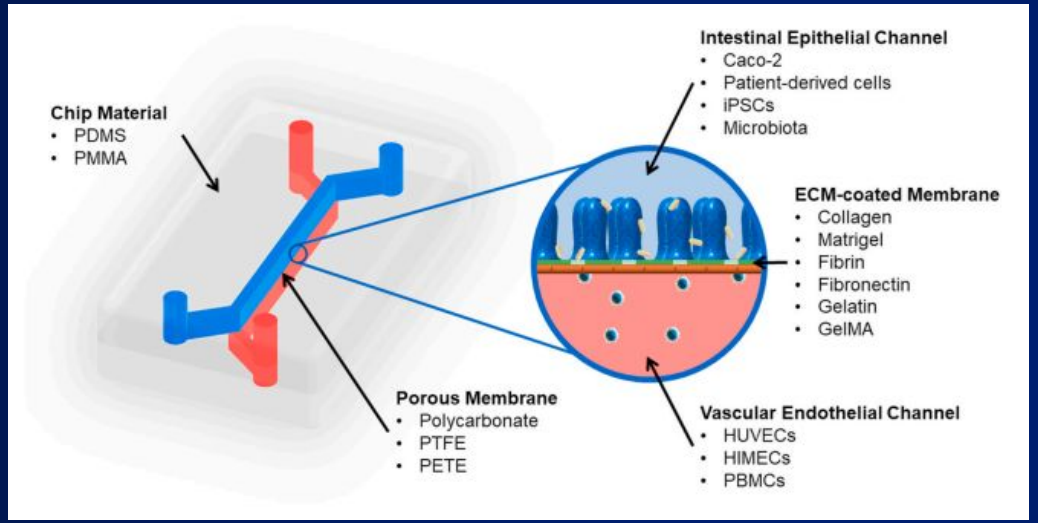
Intestinal villi and microvilli increase surface area for nutrient absorption

Mechanical

Peristaltic contractions move food through the GI tract

Ashammakhi, N., Nasiri, R., Barros, N. R., Tebon, P., Thakor, J., Goudie, M., Shamloo, A., Martin, M. G., & Khademhosseini, A. (2020). Gut-on-a-chip: Current progress and future opportunities. Biomaterials, 255. https://doi.org/10.1016/j.biomaterials.2020.120196

Existing Gut-On-A-Chip Models



- Channels and chambers
  - Sensors, electrodes, valves
- Gas permeable
- Vascular endothelial cells
- PDMS

Ashammakhi, N., Nasiri, R., Barros, N. R., Tebon, P., Thakor, J., Goudie, M., Shamloo, A., Martin, M. G., & Khademhosseini, A. (2020). Gut-on-a-chip: Current progress and future opportunities. Biomaterials, 255. https://doi.org/10.1016/j.biomaterials.2020.120196

Limitations with Current Technology

- Balance of complexity and relevance
  - Cost
  - Ease-of-use
- Incorporation of physiologically relevant cells
  - Currently use animal-derived or immortalized cell lines
  - Unable to accurately mimic *in vivo* biology
- Incorporation of biosensors and material that responds to stimuli
- Limited life span of cells on chip

Requirements for Modeling the Gut

Cellular composition

3D Architecture

Dynamic flow conditions

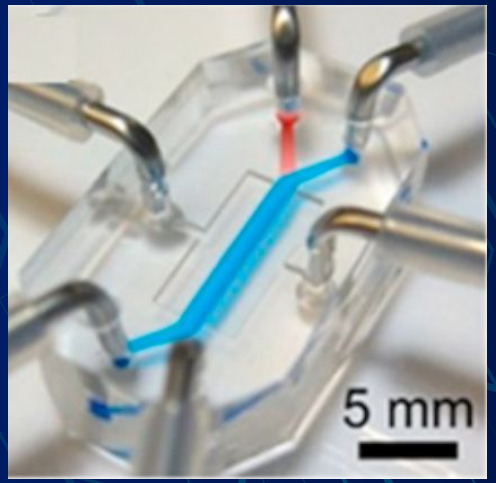
Motility

Costa J and Ahluwalia A (2019) Advances and Current Challenges in Intestinal in vitro Model Engineering: A Digest. Front. Bioeng. Biotechnol. 7:144. doi: 10.3389/fbioe.2019.00144

Proposed Solution

A gut-on-a-chip system that can diagnose food allergies and sensitivities as well as show the physiological response within the gut with less pain and high accuracy

- **What the model will achieve:**
  - ➔ A vasculature of blood vessels that will help us detect the immune cells response
  - ➔ Real time measurements of live cells and subcellular processes
  - ➔ Real mimicking of intracellular gut environment
  - ➔
- **Benefits**



Patient Specific

Time Effective

Less Painful

Predicts specific allergic reactions

Design Parameters

Geometric Confinement & Patterning

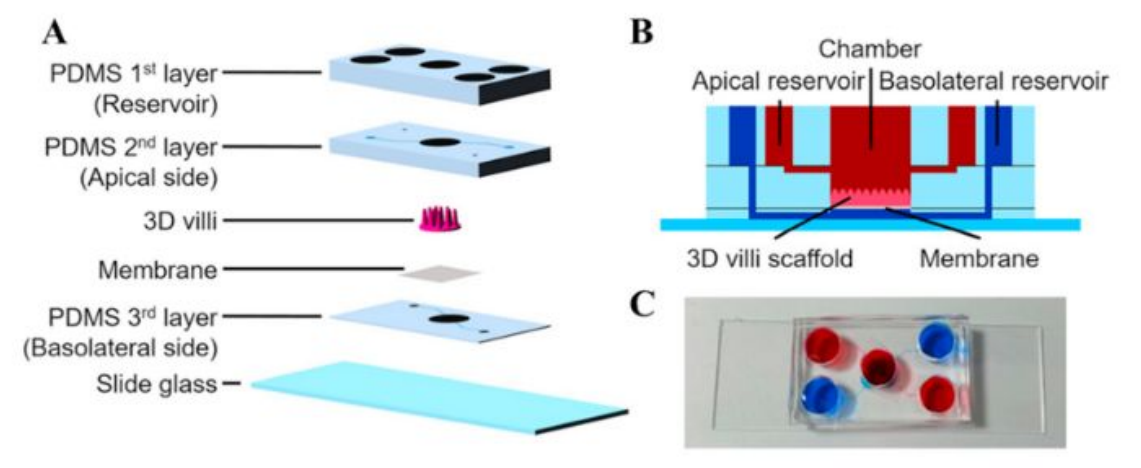
Incorporating cell samples into the chip

Mimicking real cell environment & ECM

Delivering allergen into the chip

Biosensing and physiological readouts

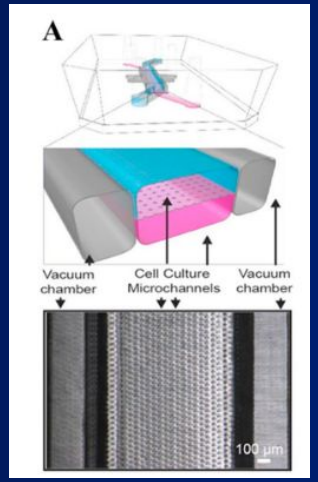
Geometric Patterning & Confinement

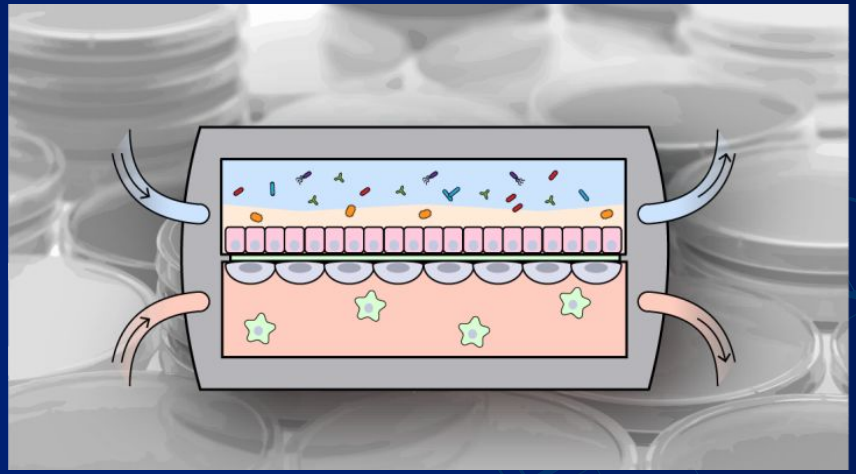


- Villi created using a dissolvable mold covered in collagen and seeded with cells (current studies use Caco-2 cells)
- Membrane composed of porous PDMS (0.45 um pore size)

Ashammakhi, N., Nasiri, R., Barros, N. R., Tebon, P., Thakor, J., Goudie, M., Shamloo, A., Martin, M. G., & Khademhosseini, A. (2020). Gut-on-a-chip: Current progress and future opportunities. Biomaterials, 255. https://doi.org/10.1016/j.biomaterials.2020.120196

Geometric Patterning & Confinement





- Endothelial cells
- Vacuum chambers assist in peristaltic movement

Ashammakhi, N., Nasiri, R., Barros, N. R., Tebon, P., Thakor, J., Goudie, M., Shamloo, A., Martin, M. G., & Khademhosseini, A. (2020). Gut-on-a-chip: Current progress and future opportunities. Biomaterials, 255. https://doi.org/10.1016/j.biomaterials.2020.120196

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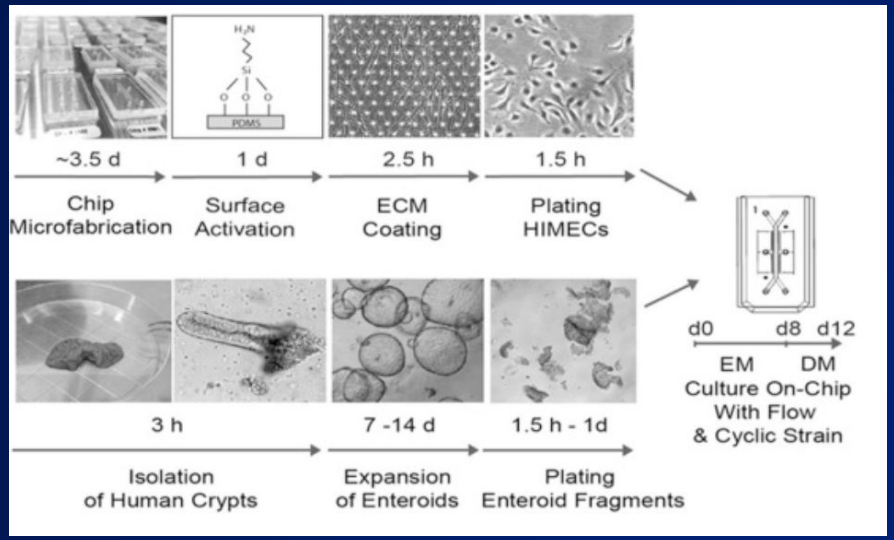
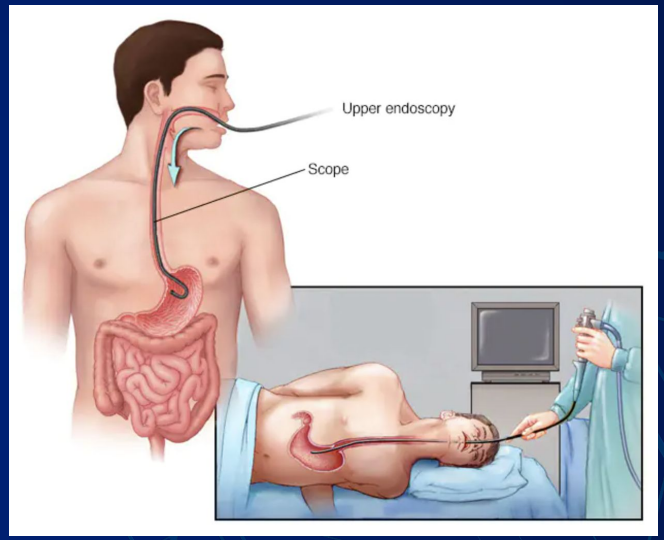
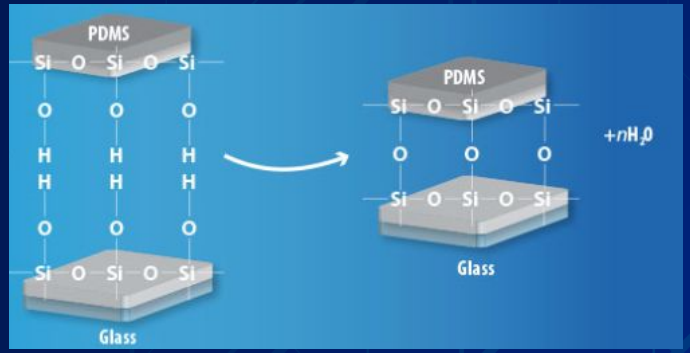
Incorporating Cell Samples into the Chip

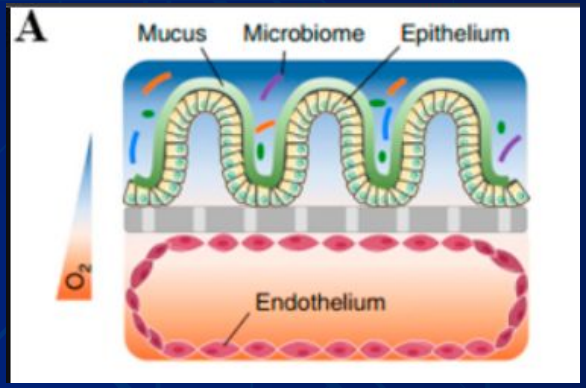




- Vascular Network
  - HUVECs or HIMECs
- Intestinal Network
  - primary human duodenal cells

Mimicking the Real Environment





- Treat the PDMS with O_2 plasma
- Increases hydrophobicity
- Decreases gas escape
- Lasts longer when kept and used in vacuum space

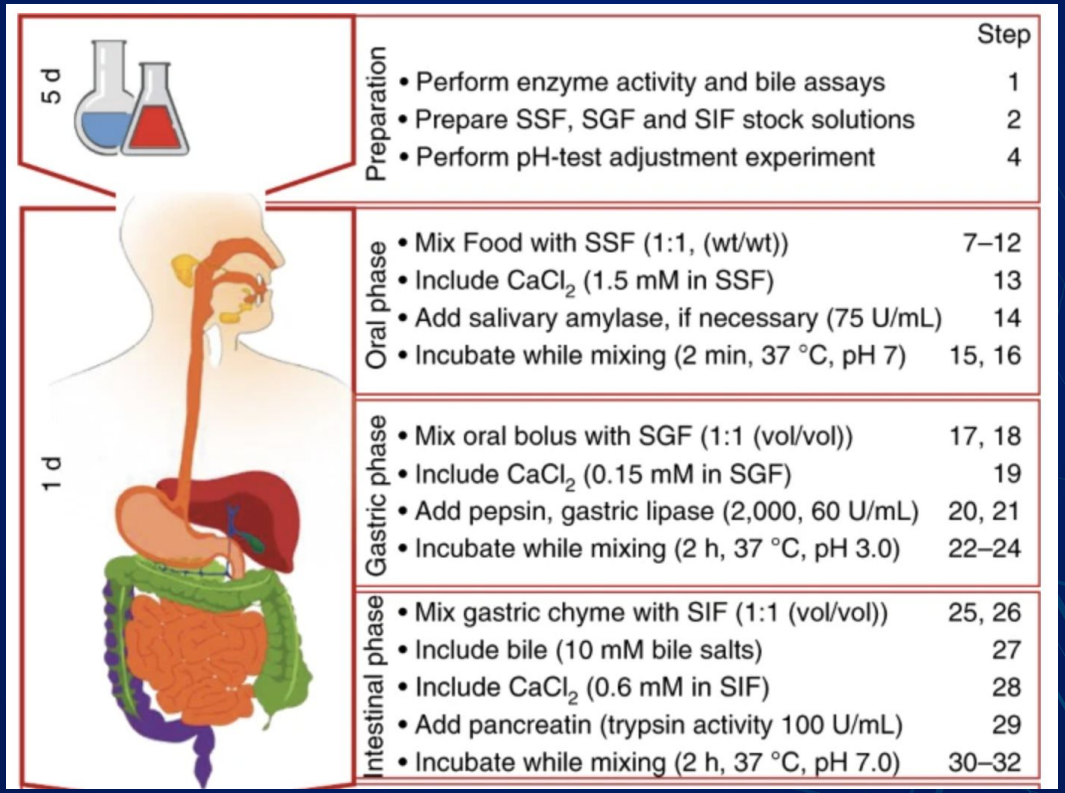
Other Features

- Lumen channel - patient's cells
- Vascular channel
- Microvilli
- Contractions

Plasma treatment of PDMS for Microfluidics. Princeton Scientific. (2019, October 16). Retrieved April 17, 2022, from https://princetonscientific.com/plasma-treatment-equipment/plasma-applications/plasma-treatment-of-pdms-for-microfluidics/
Ashammakhi, N., Nasiri, R., Barros, N. R., Tebon, P., Thakor, J., Goudie, M., Shamloo, A., Martin, M. G., & Khademhosseini, A. (2020). Gut-on-a-chip: Current progress and future opportunities. Biomaterials, 255. https://doi.org/10.1016/j.biomaterials.2020.120196

Delivering Allergens

- Need to digest the food that is being tested and then deliver this into the intestinal channel



BioSensing and Physiological Readouts

Biomarkers:

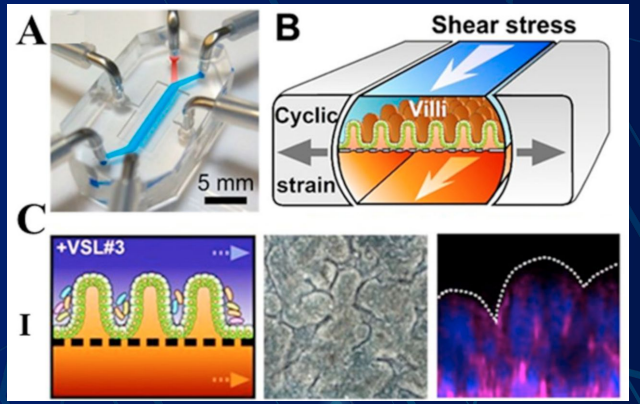
- There's not yet a single universal biomarker to diagnose food allergies.
- Ideal: detect the different biomarkers simultaneously to effectively track the disease

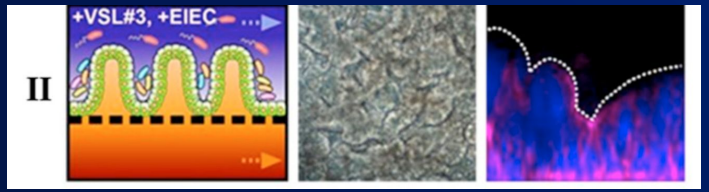
Cytokine Release and inflammation:

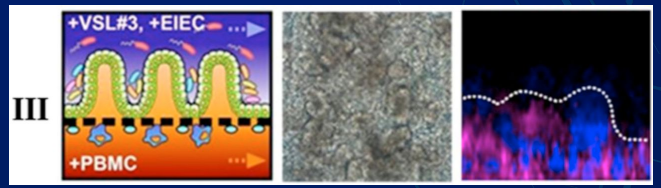
Immune cells produce proinflammatory cytokines in response to allergen presence

Cyclic mechanical strain and shear stress induced on the villi due to inflammation

Visualize: fluorescent micrographs and phase contrast images



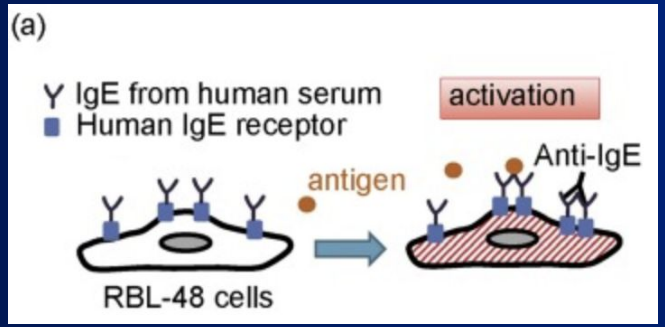


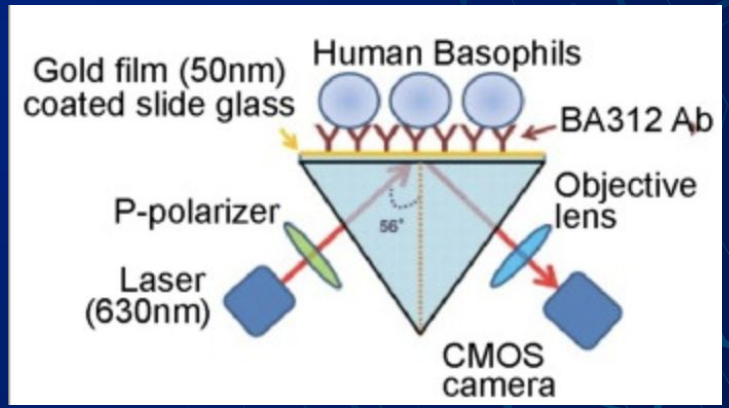


Ashammakhi, Nureddin, et al.

Surface Plasmon Resonance

- Examine sensitive changes to optical properties induced by intracellular changes like morphological changes and cell adhesion
- Cell degranulation
- Fix basophils with BA312 antibodies to the sensor surface and capture the change in intensity and in cell refractive index upon activation in real time.





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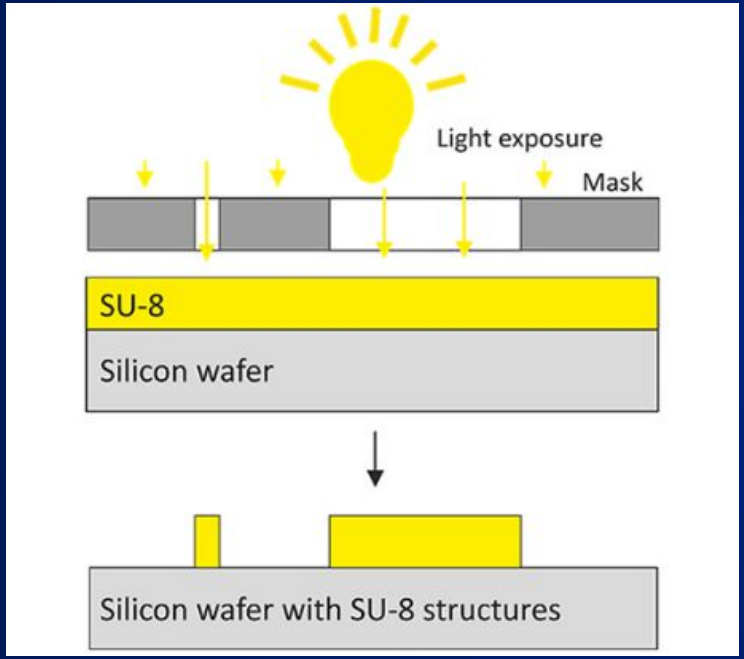
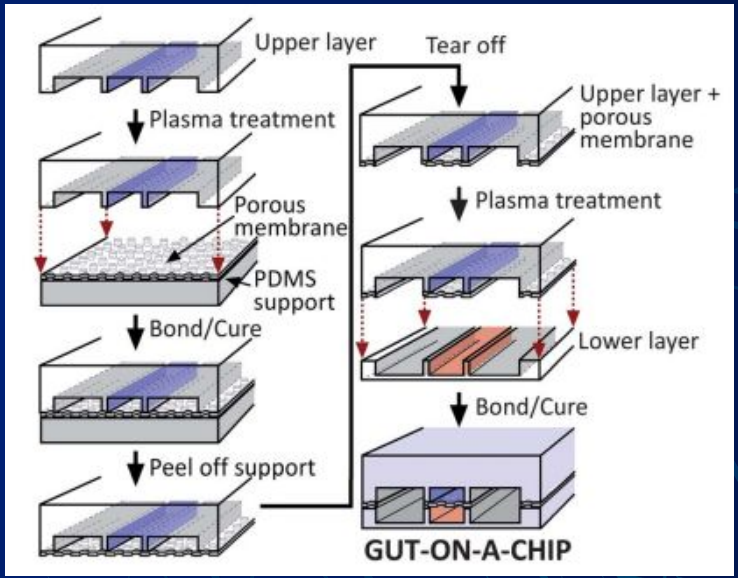
Fabrication





Elsbeth G.B.M. Bossink, Loes I. Segerink, Mathieu Odijk, Organ-on-Chip Technology for Aerobic Intestinal Host – Anaerobic Microbiota Research, Organs-on-a-Chip, Volume 4, 2022, 100013, ISSN 2666-1020, https://doi.org/10.1016/j.ooc.2021.100013.

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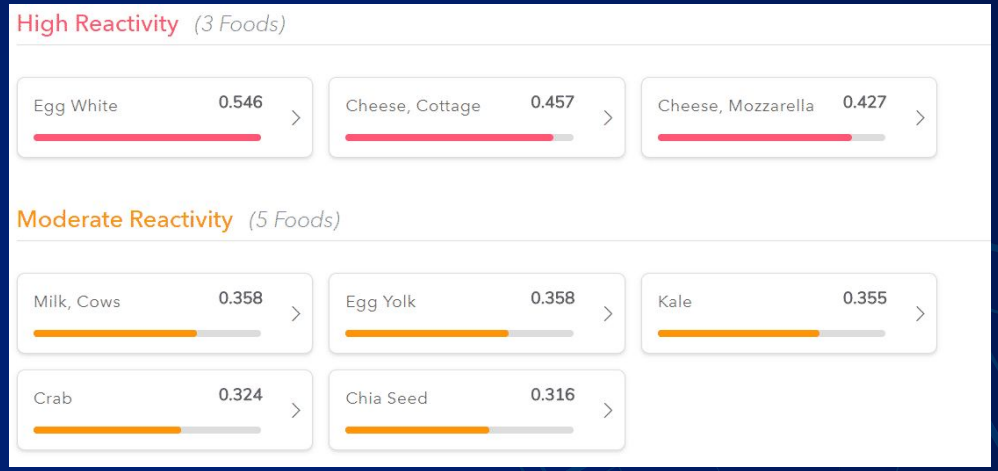
Testing

EverlyWell Test Results



- Compare to food sensitivity tests or elimination diets
- Compare immune response to reactions from other allergens (same patient)
- Variety of tests to verify the results

Limitations

1. Sourcing cells from specific patients to test
2. Cost
3. Time to Manufacture
4. Does not account for interaction with other organ systems

Summary

- New gut-on-a-chip model to test for food allergies and intolerances
- Combine characteristics from existing chip models
- Specialize each chip to each patient

Questions

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