Johns Hopkins Engineering

Immunoengineering

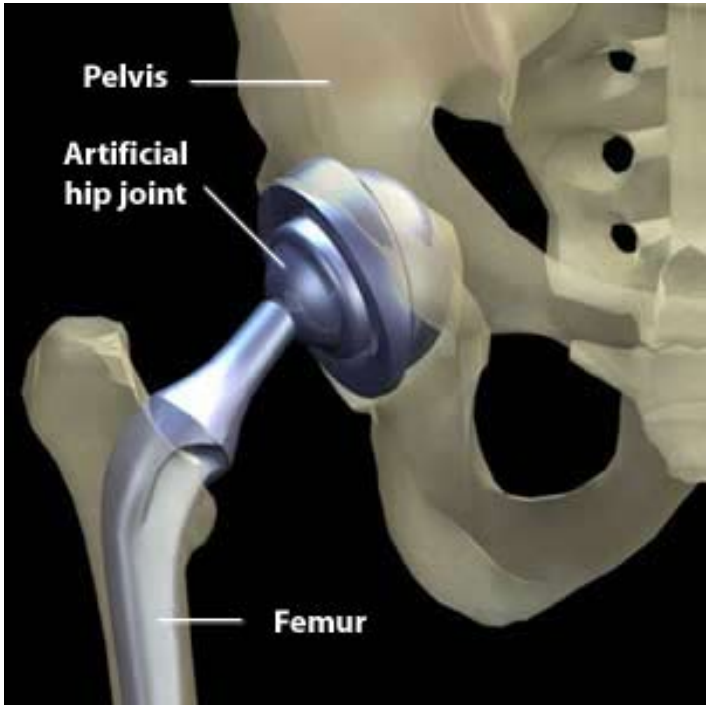
Module 1/Lecture 1B

Immunoengineering: A New Frontier

Opportunities and Challenges

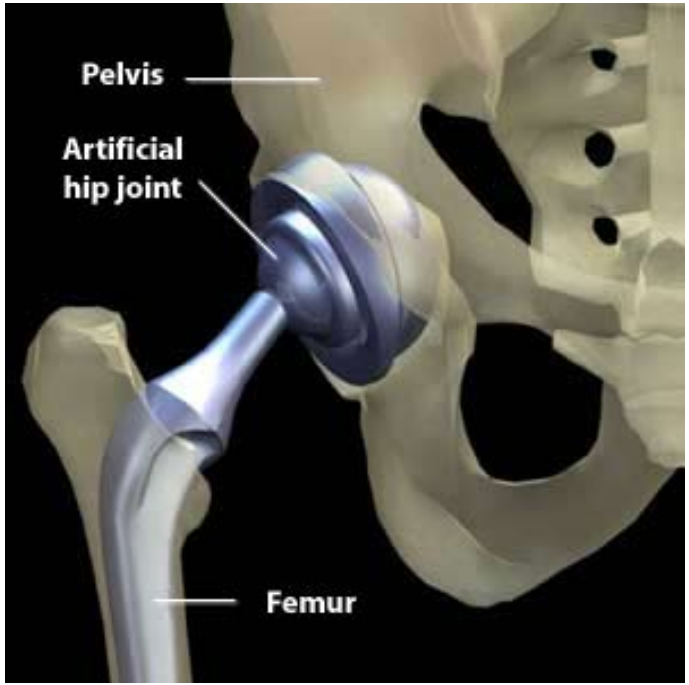
JOHNS HOPKINS
WHITING SCHOOL
of ENGINEERING

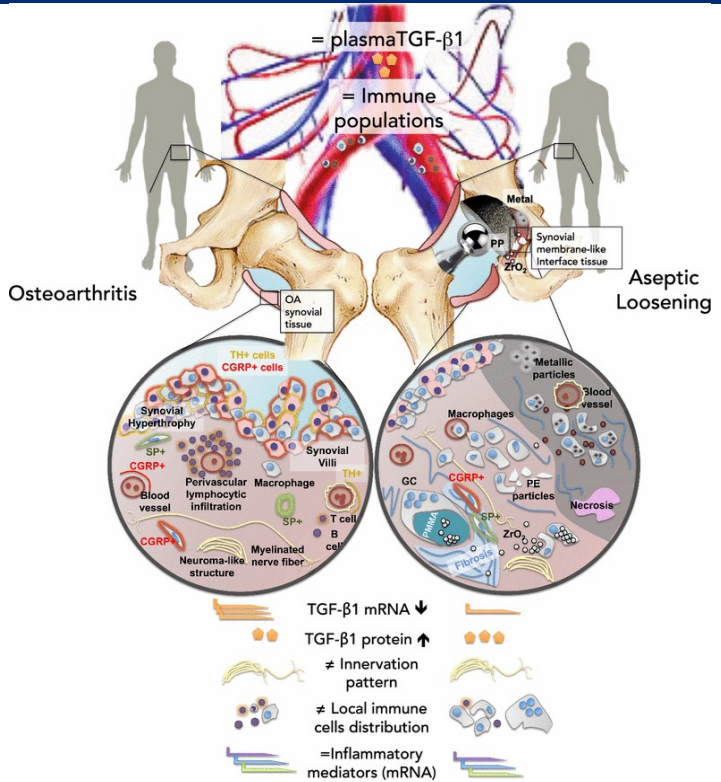
Immune Response to Biomaterials



Artificial hip joint. http://www.medtouradvisor.com/joint-replacement-surgeries/

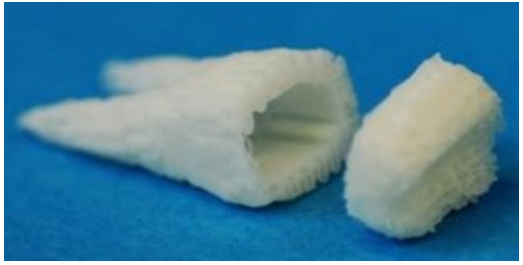
Immune Response to Biomaterials: Material Properties

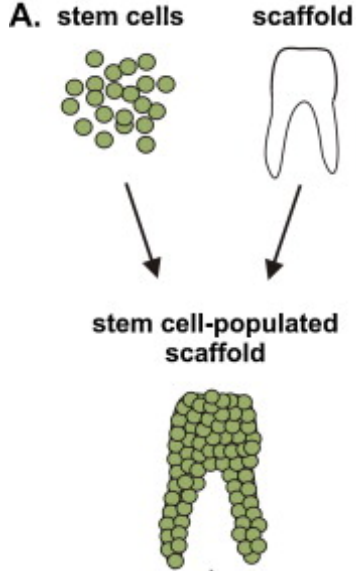




Vasconcelos, Daniel M., et al. "Immune response and innervation signatures in aseptic hip implant loosening." Journal of translational medicine 14.1 (2016): 20

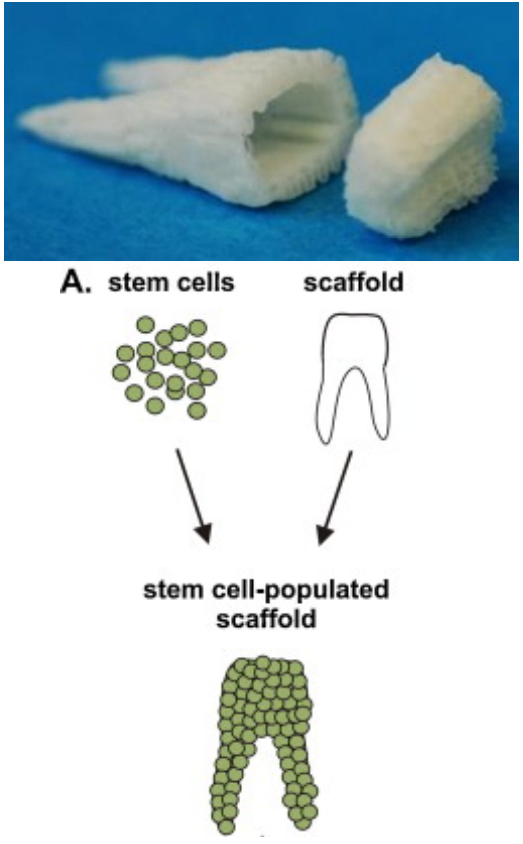
Immune Response to Biomaterials

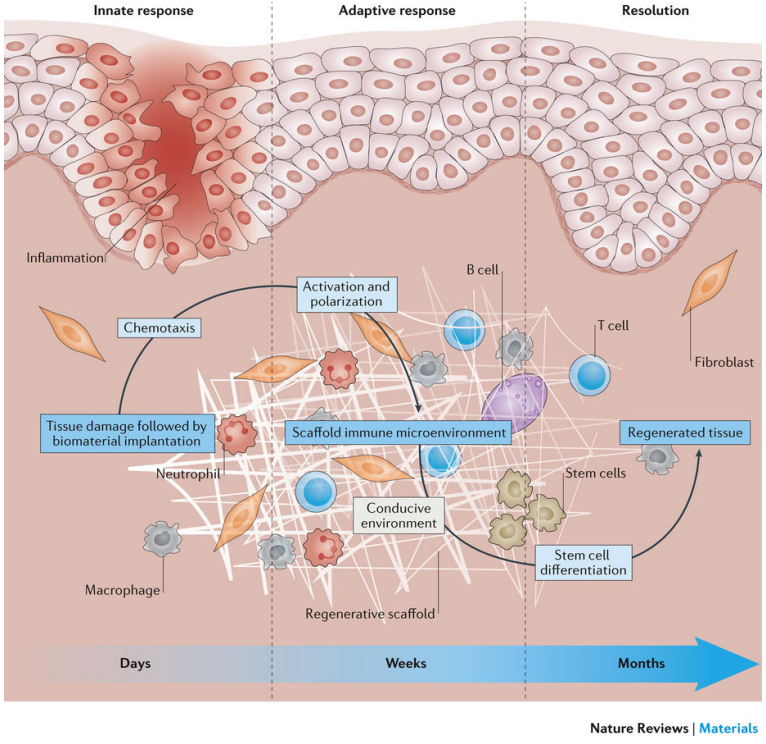




http://thefutureofthings.com/4335-growing-dental-implants-in-place/,
Steindorff, Marina M., et al. "Innovative approaches to regenerate teeth by tissue engineering." Archives of oral biology 59.2 (2014): 158-166.,

Immune Response to Biomaterials: Tissue Regeneration





Sadtler, Kaitlyn, et al. "Design, clinical translation and immunological response of biomaterials in regenerative medicine." *Nature Reviews Materials* 1 (2016): 16040.

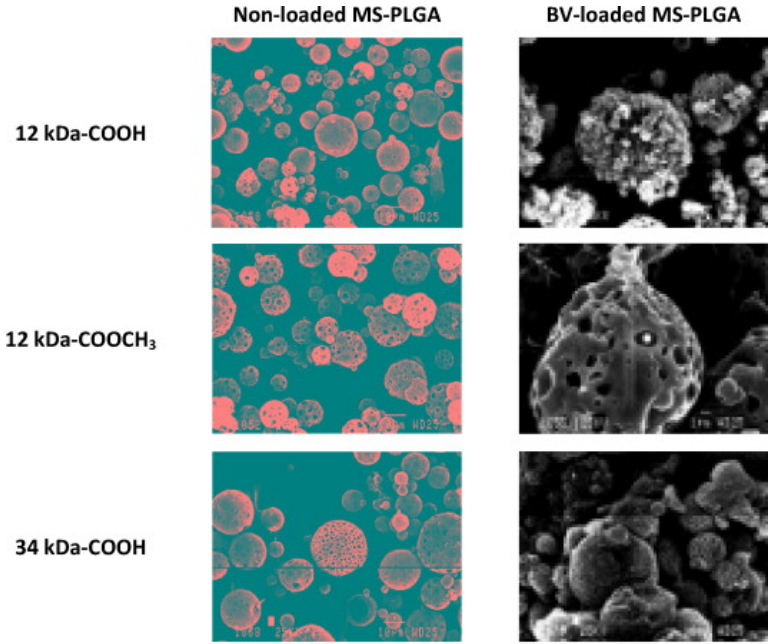
Allergy Immune Response

Wasp sting with a droplet of venom

https://en.wikipedia.org/wiki/Venom#/media/File:Waspstinger1658-2.jpg

Allergy Immune Response

Wasp sting with a droplet of venom



Effect of molecular mass and carboxy-terminal (free or methylated) on the morphology of MS-PLGA by SEM (1000×)

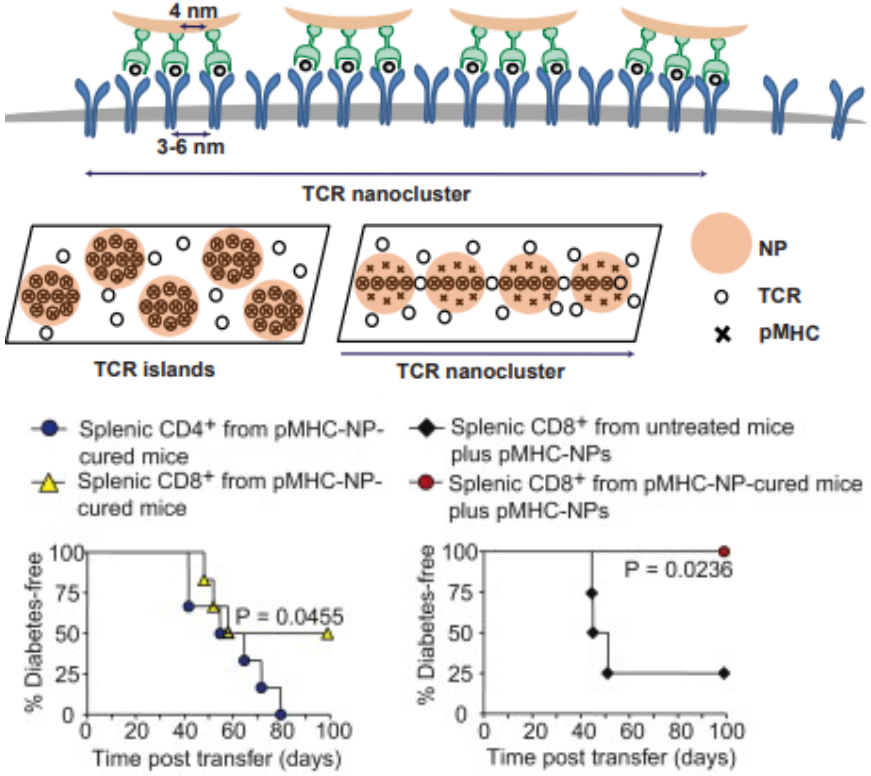
Trindade, Reginaldo A., et al. "PLGA microspheres containing bee venom proteins for preventive immunotherapy." *International journal of pharmaceutics* 423.1 (2012): 124-133.

Autoimmune Response

Glucose monitoring

Glucose monitoring. https://en.wikipedia.org/wiki/Blood_glucose_monitoring

Autoimmune Response: Cell Engineering

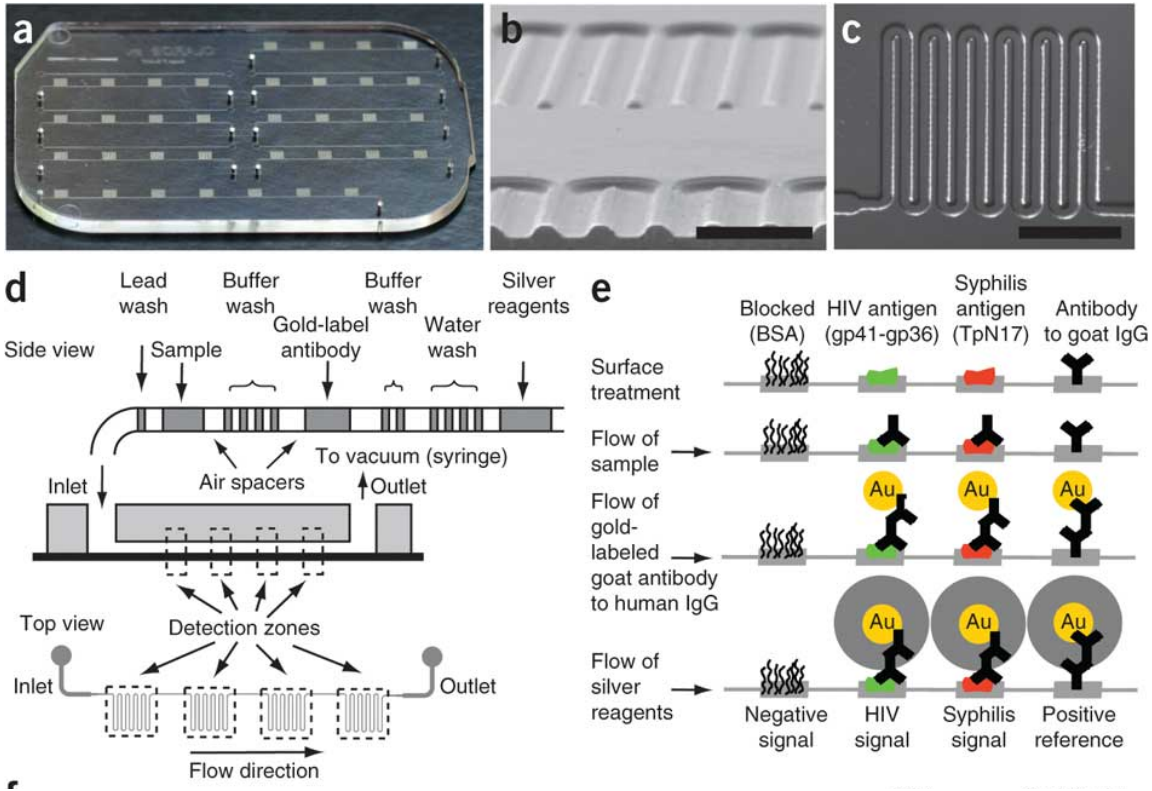


Singha, Santiswarup, et al. "Peptide-MHC-based nanomedicines for autoimmunity function as T-cell receptor microclustering devices." *Nature Nanotechnology* 12 (2017): 701-710

Immune Response to Pathogens

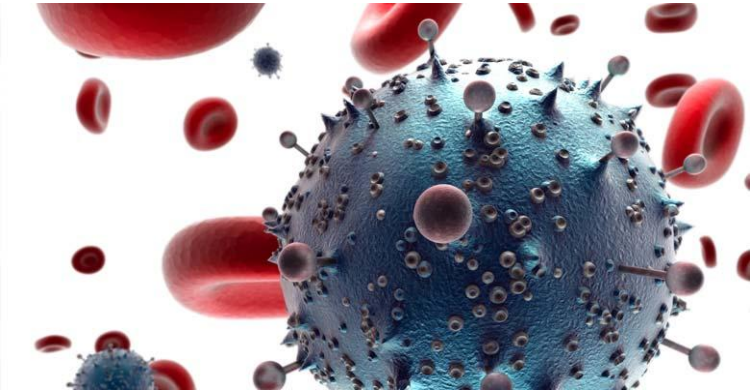
https://www.clintonfoundation.org/blog/2014/12/01/improving-access-viral-load-testing-hiv-patients-developing-countries

Immune Response to Pathogens: Imaging/Detection



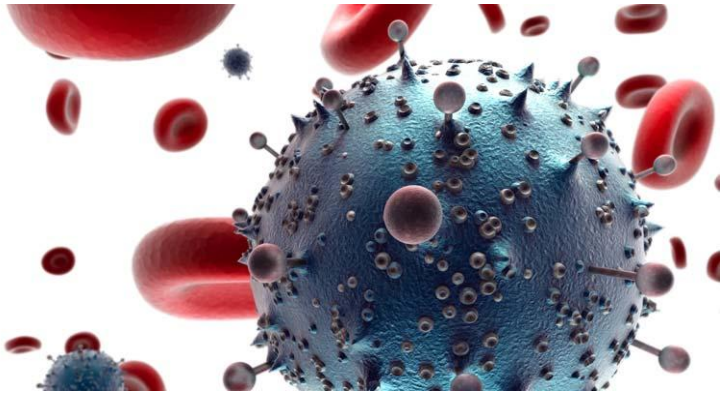
Chin, Curtis D., et al. "Microfluidics-based diagnostics of infectious diseases in the developing world." *Nature medicine* 17.8 (2011): 1015-1019.

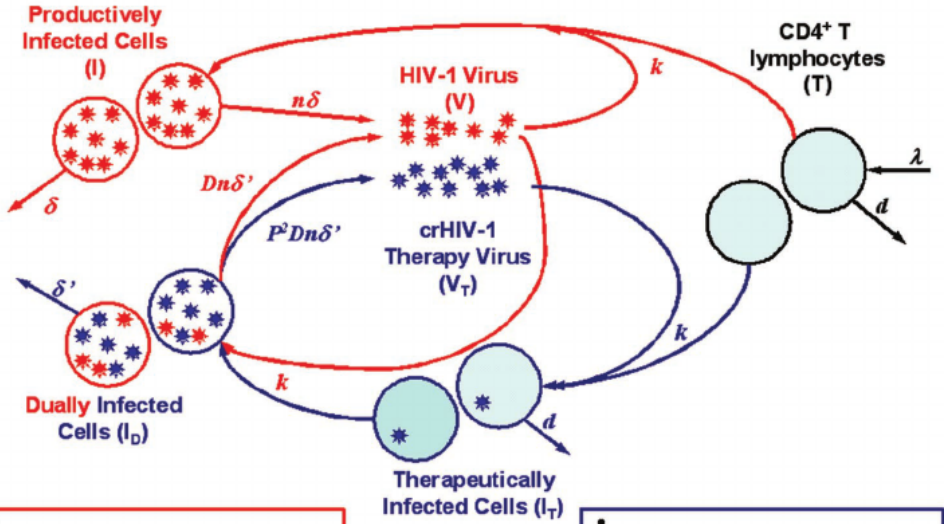
Immune Response to Pathogens



https://www.avert.org/professionals/hiv-science/overview

Immune Response to Pathogens: Mathematical Modeling





$$\dot{T} = \lambda - dT - kVT - kV_T T \quad [1]$$

$$\dot{I} = kVT - \delta I \quad [2]$$

$$\dot{V} = n\delta I - cV + Dn\delta' I_D \quad [3]$$

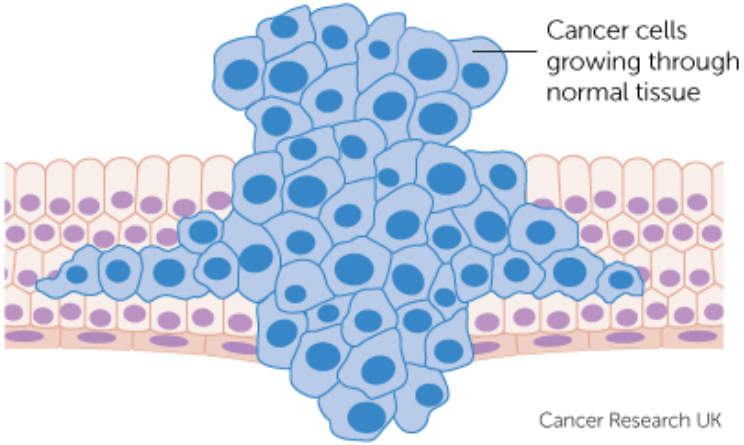
$$\dot{I}_T = kV_T T - dI_T - kVI_T \quad [4]$$

$$\dot{I}_D = kVI_T - \delta' I_D \quad [5]$$

$$\dot{V}_T = P^2 Dn\delta' I_D - cV_T \quad [6]$$

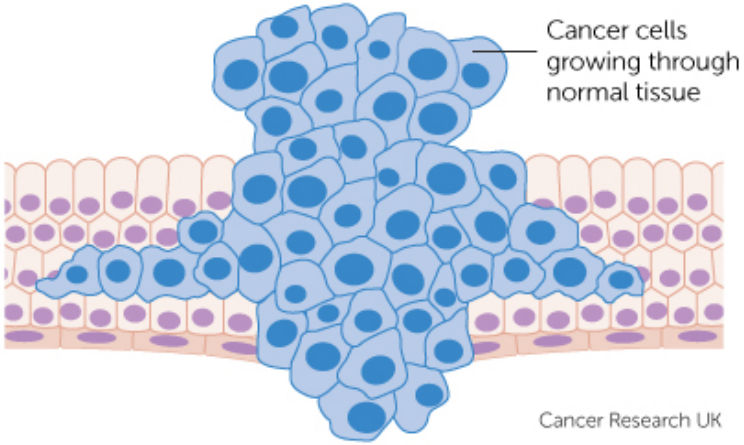
Weinberger, Leor S., David V. Schaffer, and Adam P. Arkin. "Theoretical design of a gene therapy to prevent AIDS but not human immunodeficiency virus type 1 infection." *Journal of virology* 77.18 (2003): 10028-10036.

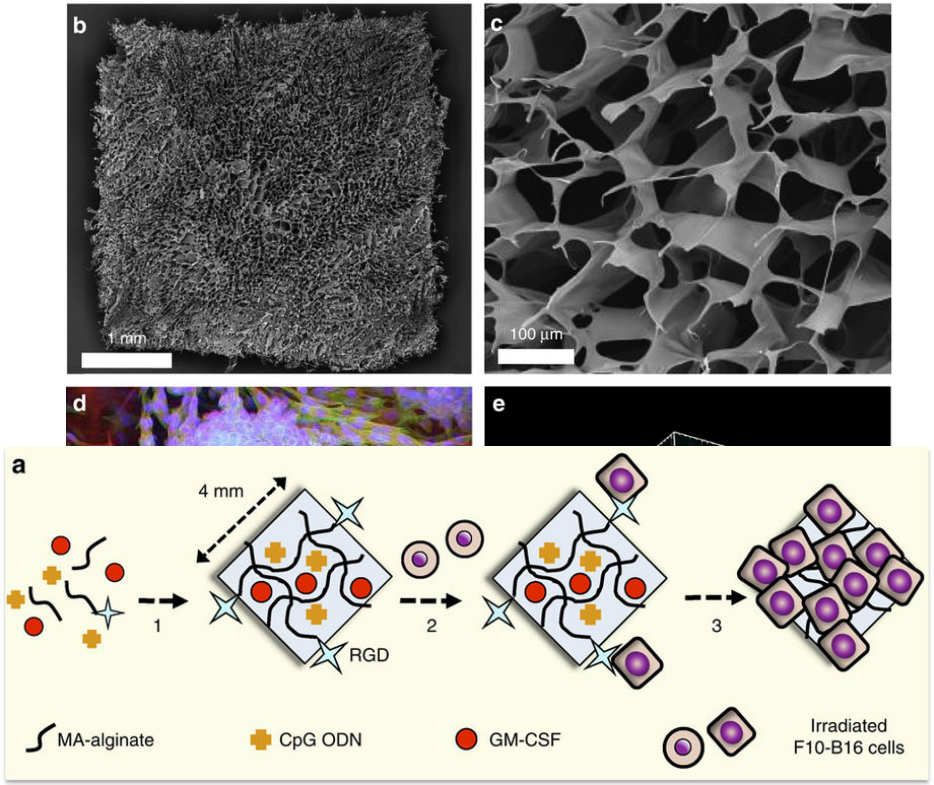
Immune Response to Cancer



http://www.cancerresearchuk.org/about-cancer/what-is-cancer

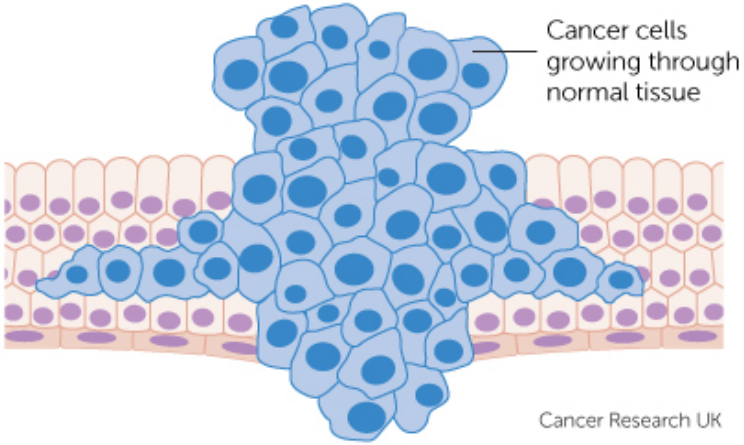
Immune Response to Cancer: Materials Science





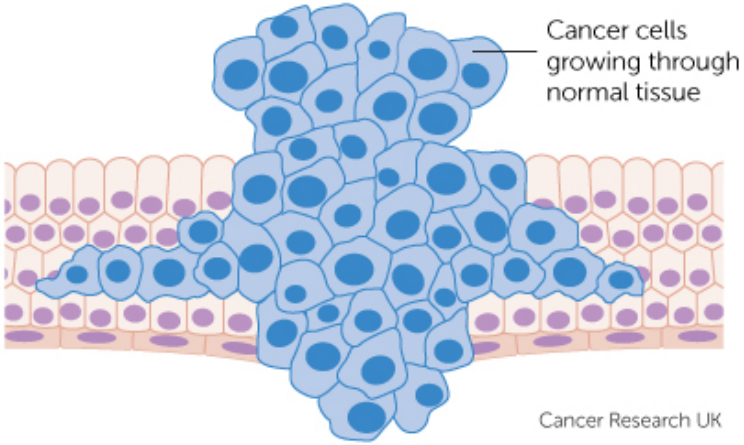
Bencherif, Sidi A., et al. "Injectable cryogel-based whole-cell cancer vaccines." Nature communications 6 (2015).

Immune Response to Cancer



http://www.cancerresearchuk.org/about-cancer/what-is-cancer

Immune Response to Cancer: Protein Engineering



https://www.ohcare.com/ohc-approval-of-nivolumab-first-lung-cancer-immunotherapy/, https://scienceofparkinsons.com/tag/treg/,

Boom Times

Immune-engineering startups have gone public, raising large sums for human trials.

Company	Amount Raised in IPO	Date
Kite Pharma	$134 million	June 2014
Juno Therapeutics	$304 million	December 2014
Bellicum Pharmaceuticals	$160 million	December 2014
Cellectis	$228 million	March 2015

https://www.technologyreview.com/s/600763/10-breakthrough-technologies-2016-immune-engineering/, http://epivax.com/, http://vedantra.com/, , https://www.medimmune.com/, , http://www.neximmune.com/, http://www.parvustherapeutics.com/

Challenges Facing Immunoengineering

http://immunoengineering.gatech.edu/

Challenges Facing Immunoengineering

- Overengineering the immune response

NATURE BIOTECHNOLOGY | NEWS

CAR-T death strikes Kite

Nature Biotechnology **35**, 492 (2017) | doi:10.1038/nbt0617-492
Published online 07 June 2017

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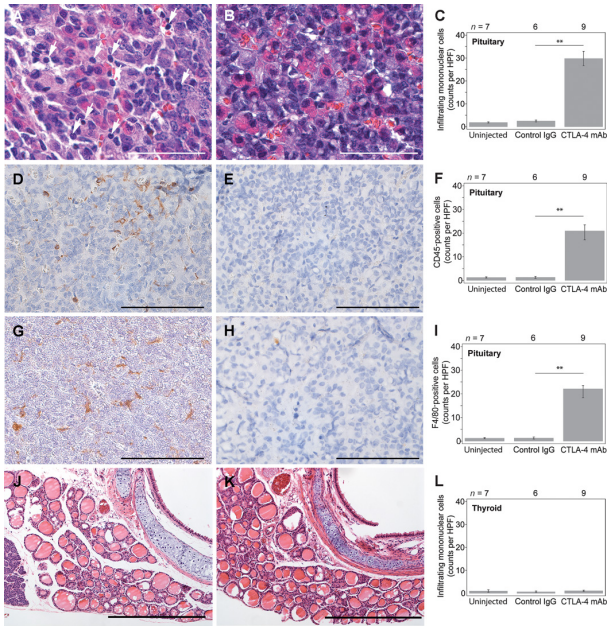
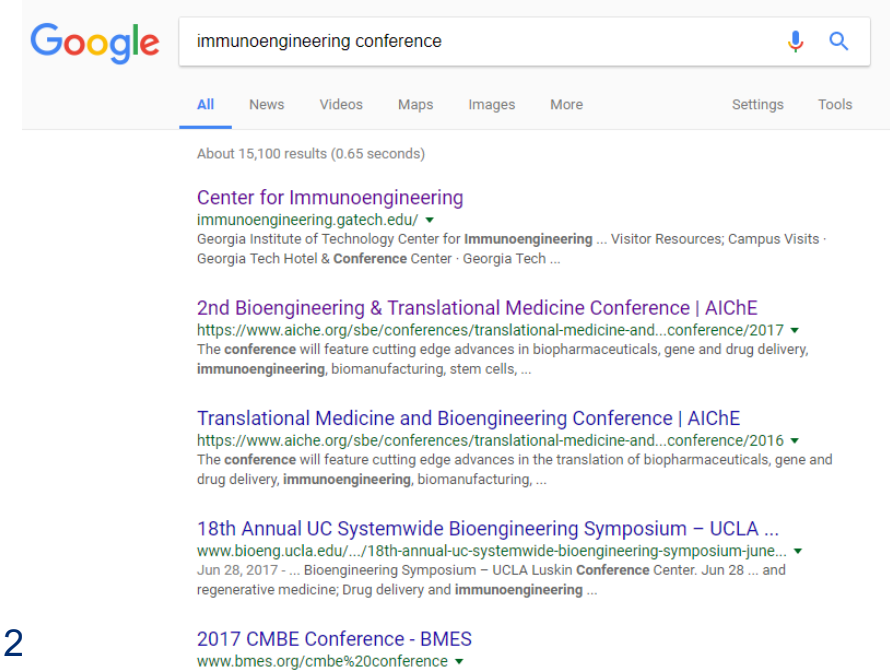
Kite Pharma's shares plunged on May 8 after news spread that a patient in a safety study testing a chimeric antigen receptor (CAR)-T cell therapy to treat non-Hodgkin's lymphoma (NHL) had died. The patient in the phase 2 ZUMA-1 study testing axicabtagene ciloleucel (KTE-19) developed fatal cerebral edema, a situation resembling a setback experienced last year by rival CAR-T cell therapy developer Juno, when five patients treated with its candidate product JCAR015, a CD19- targeted CAR-T product for treating relapsed refractory acute lymphoblastic leukemia (*Nat. Biotechnol.* **35**, 6–7, 2017), died. The deaths led Juno to drop the program. Investors may have been rattled by Kite's news, because there are similarities between the two treatments: both Kite's KTE-19 and JCAR015 target CD19 and use the CD28 co-stimulatory domain. Kite has informed the US Food and Drug Administration of the event and all studies of the candidate drug will continue as planned. Kite's chief medical officer David Chang said the patient had "explosive disease and was rapidly progressing" at the time of enrollment, and that this was the only death in 300 patients treated with KTE-19. In March, Kite completed a Biologics License Application for this therapy in relapsed or refractory aggressive NHL. Basel, Switzerland–based Novartis also submitted a biologics license application under priority review for another

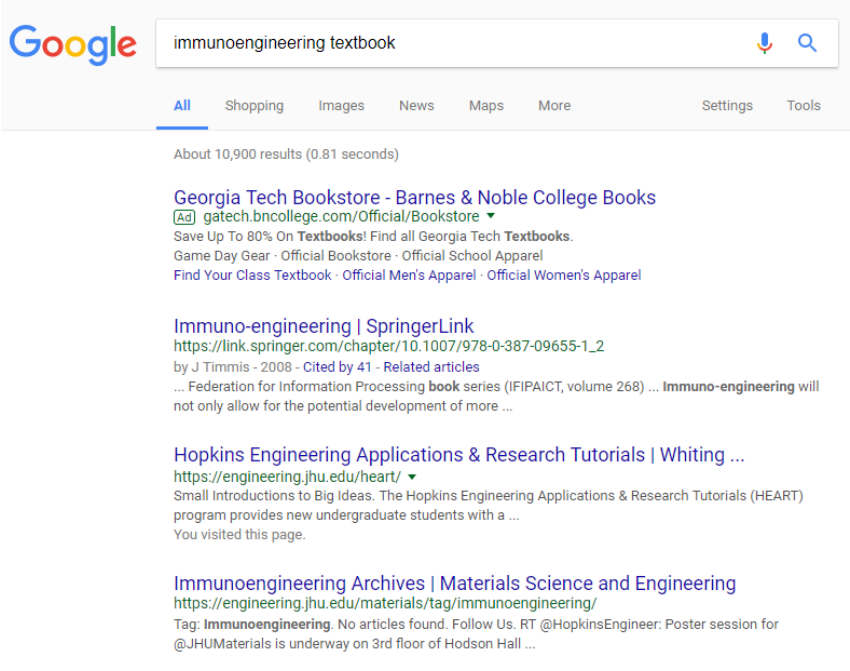


Senior, Melanie. "CAR-T death strikes Kite." Technology Review (2017)., Iwama, Shintaro, et al. "Pituitary expression of CTLA-4 mediates hypophysitis secondary to administration of CTLA-4 blocking antibody." Science translational medicine 6.230 (2014): 230ra45-230ra45.,

Challenges Facing Immunoengineering

- Overengineering the immune response
- Ineffective cross-communication





Challenges Facing Immunoengineering

- Overengineering the immune response
- Ineffective cross-communication
- Lack of uniformity

NATURE REVIEWS IMMUNOLOGY | PERSPECTIVES | ESSAY

Immunity by equilibrium

Gérard Eberl

Nature Reviews Immunology **16**, 524–532 (2016) | doi:10.1038/nri.2016.75
Published online 11 July 2016

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Abstract

Abstract • References • Author information

Eberl, Gérard. "Immunity by equilibrium." *Nature Reviews Immunology*(2016).