Johns Hopkins Engineering

Immunoengineering

Immunoengineering: Biomaterials and Tissue Engineering

Mitigating the Foreign Body Reaction

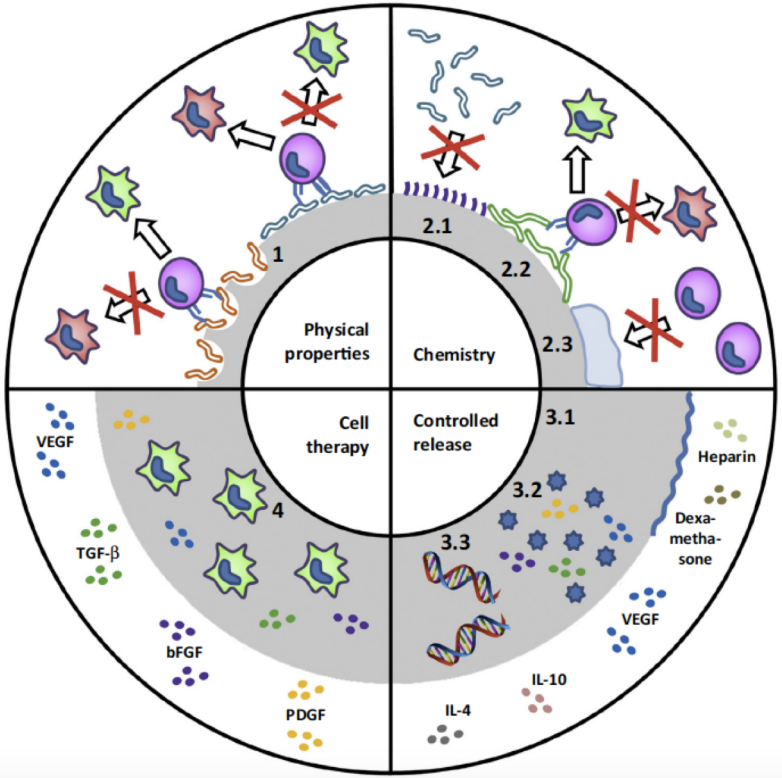
JOHNS HOPKINS
WHITING SCHOOL
of ENGINEERING

Foreign Body Reaction (FBR)

- Inflammatory response that leads to excessive fibrous encapsulation of implant
- Leads to impaired implant/device function and failure
- Prevents biomaterial/implant interaction and integration with body

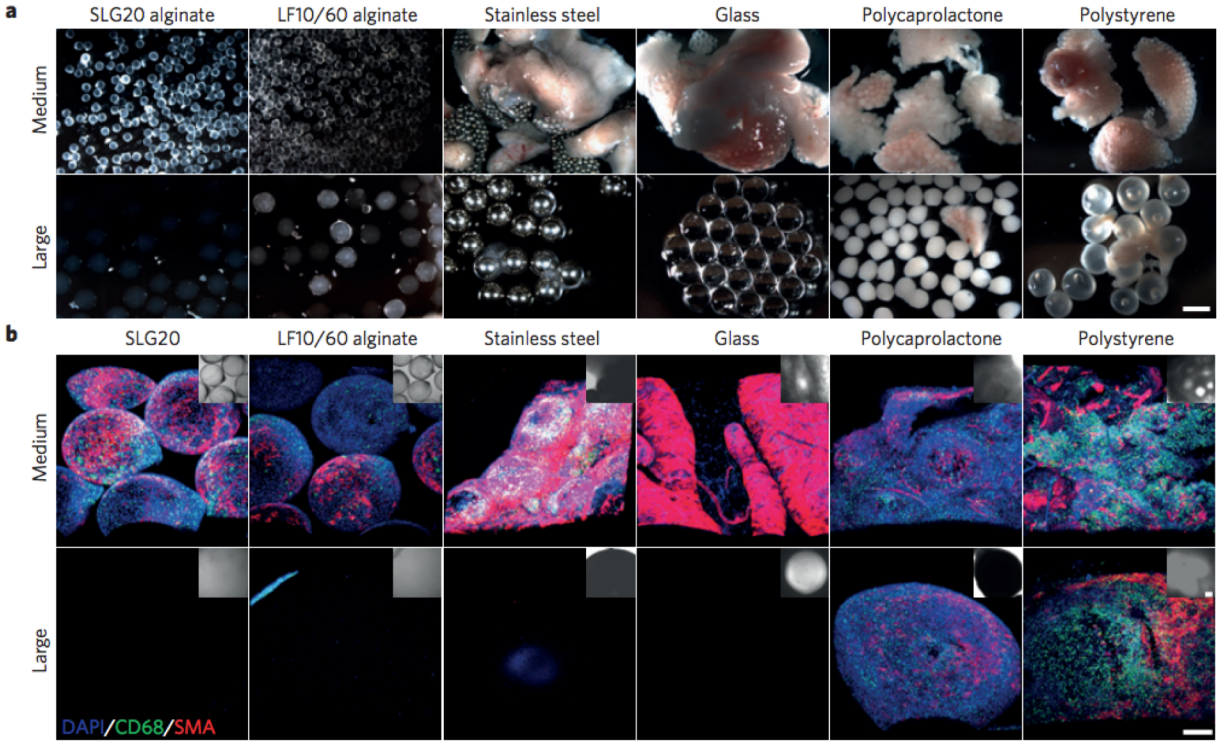
Engineering Strategies to Reduce FBR

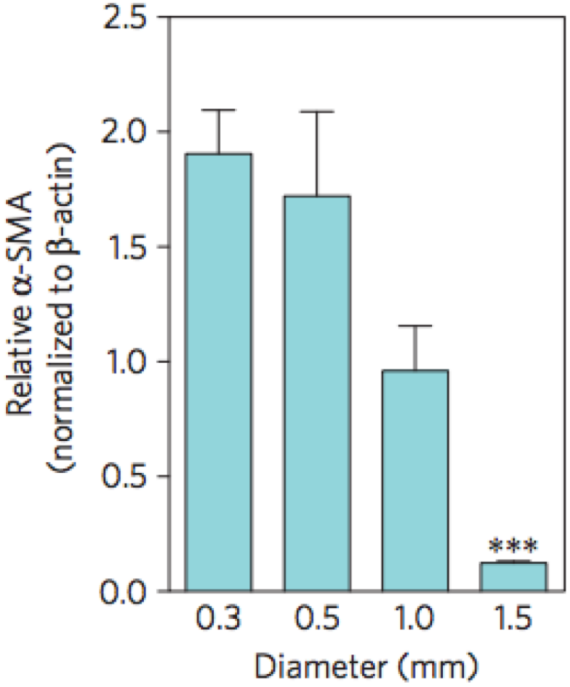
- Physical parameters
  - Stiffness, topography
- Surface properties
- Delivery of anti-inflammatory molecules
- Incorporation of immune cells



Vishwakarma et al. "Engineering Immunomodulatory Biomaterials To Tune the Inflammatory Response" *Trends in Biotechnology,* 34(6), (2016): 470-482.

Physical properties: size



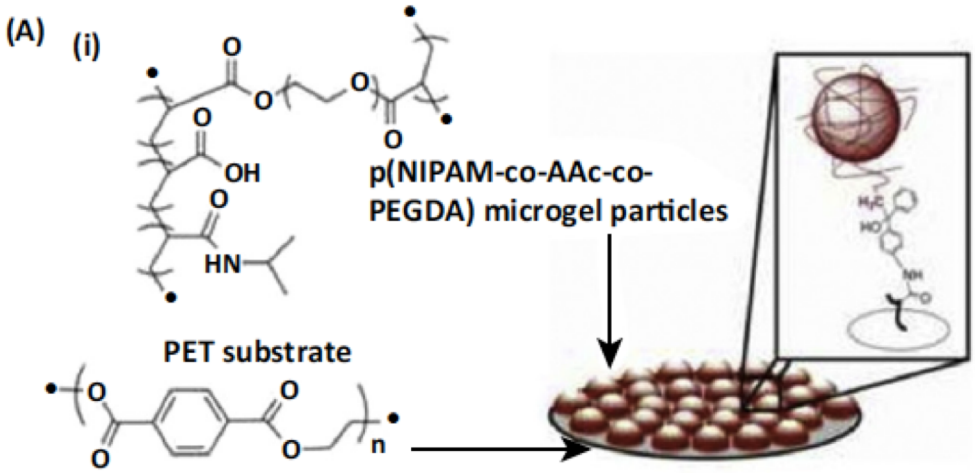


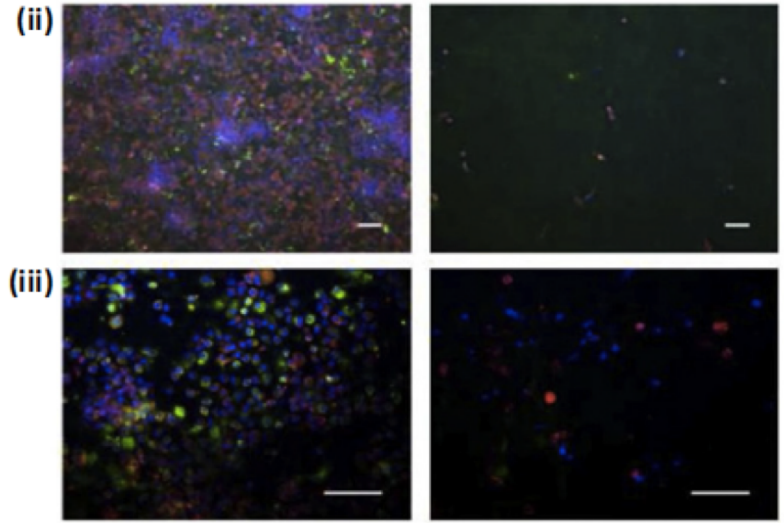
Veiseh et al. “Size- and shape-dependent foreign body immune response to materials implanted in rodents and non-human primates” *Nature Materials* 14, (2015): 643-652.

Other physical properties

- Shape
  - Smooth, well-contoured surfaces have reduced FBR compared to implants with sharp features (e.g. corners, acute angles)
- Topography
  - E.g. titanium implants with nano/micro roughness have reduced FBR
- Porosity

Surface properties: non-fouling coatings



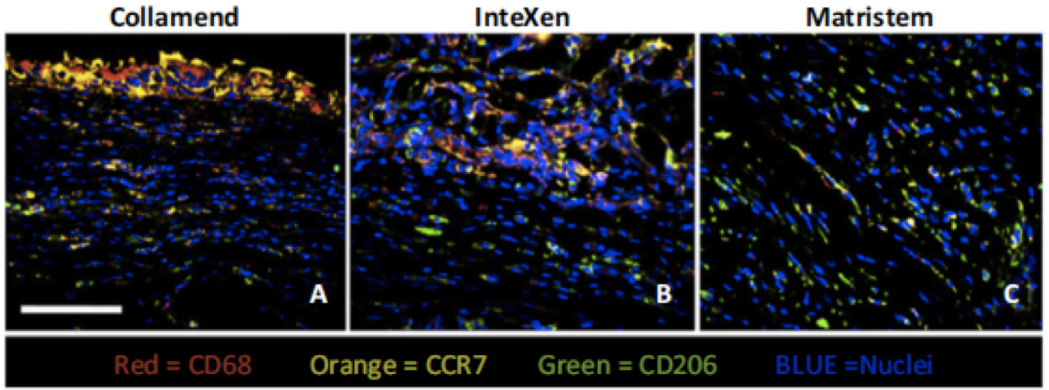


Vishwakarma et al. “Engineering Immunomodulatory Biomaterials To Tune the Inflammatory Response” *Trends in Biotechnology,* 34(6), (2016): 470-482.

Surface properties: extracellular matrix (ECM)

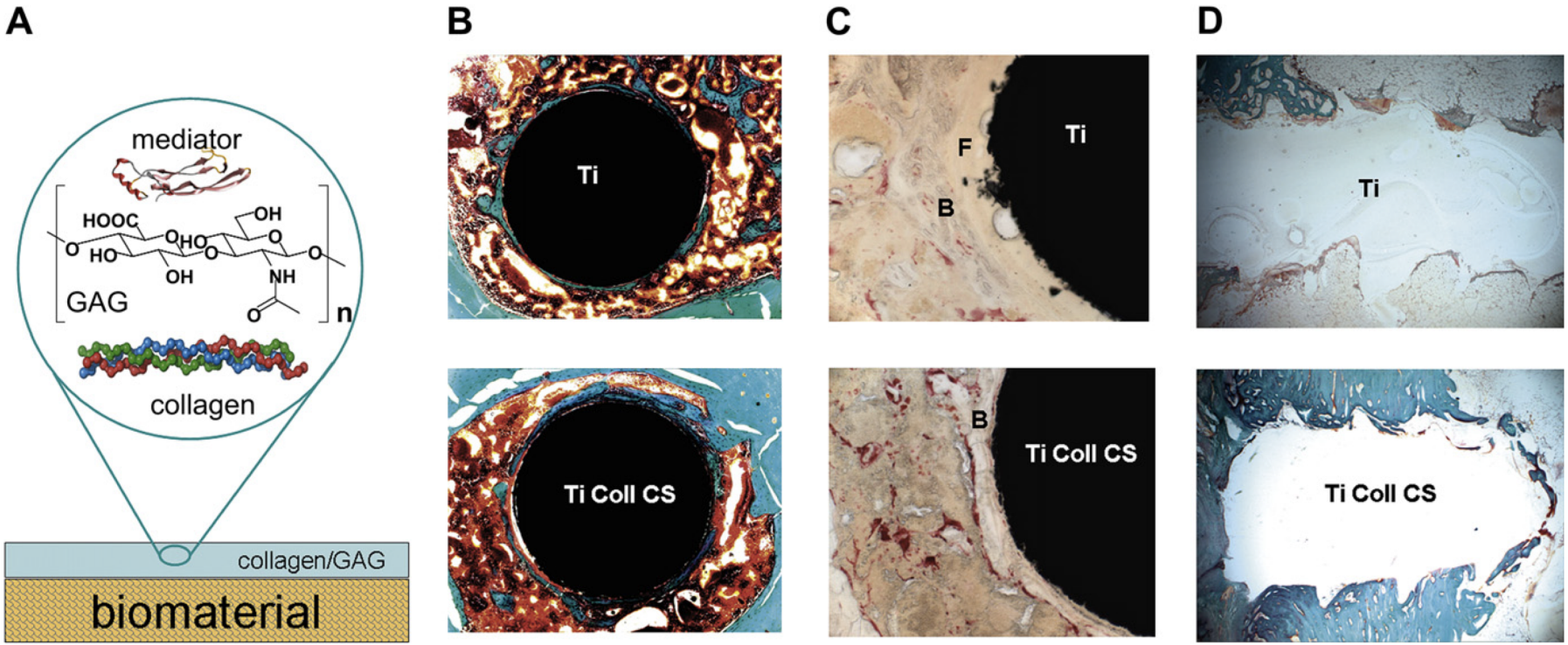
Table 1
Name, manufacturer and composition of the biologically derived surgical mesh materials examined.

Test article	Manufacturer	Composition
AlloMax	C. R. BARD, Inc.	Human dermis
AlloDerm	LifeCell Corporation	Human dermis
Avaulta Plus	C. R. BARD, Inc.	Porcine dermis (cross-linked)
CollaMend	C. R. BARD, Inc.	Porcine dermis (cross-linked)
Flex HD	Ethicon, Inc.	Human dermis
InteXen LP	American Medical Systems	Porcine dermis
MatriStem	Acell, Inc.	Porcine urinary bladder (4 layer)
PelviSoft	C. R. BARD, Inc.	Porcine dermis (cross-linked)
Strattice Firm	LifeCell Corporation	Porcine dermis
Strattice Pliable	LifeCell Corporation	Porcine dermis
Sugisis	Cook Medical	Porcine small intestinal submucosa (8 layer)
SurgiMend	TEI Biosciences, Inc.	Fetal bovine dermis
Veritas	Synovis Life Technologies, Inc.	Bovine pericardium
Xenform	Boston Scientific Corporation	Fetal bovine dermis



Brown et al. “Macrophage phenotype as a predictor of constructive remodeling following the implantation of biologically derived surgical mesh materials” *Acta Biomaterialia* 8, (2012): 978-987.

Surface properties: ECM coating



Franz et al. “Immune responses to implants – A review of the implications for the design of immunomodulatory biomaterials” *Biomaterials* 32, (2011): 6692-6709.

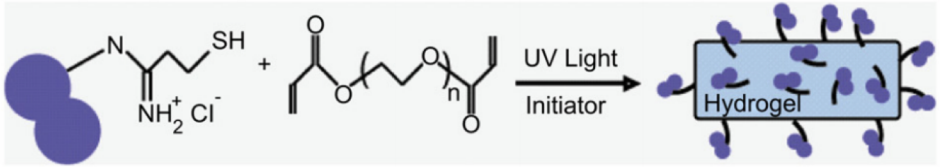
Biomaterial physicochemical properties

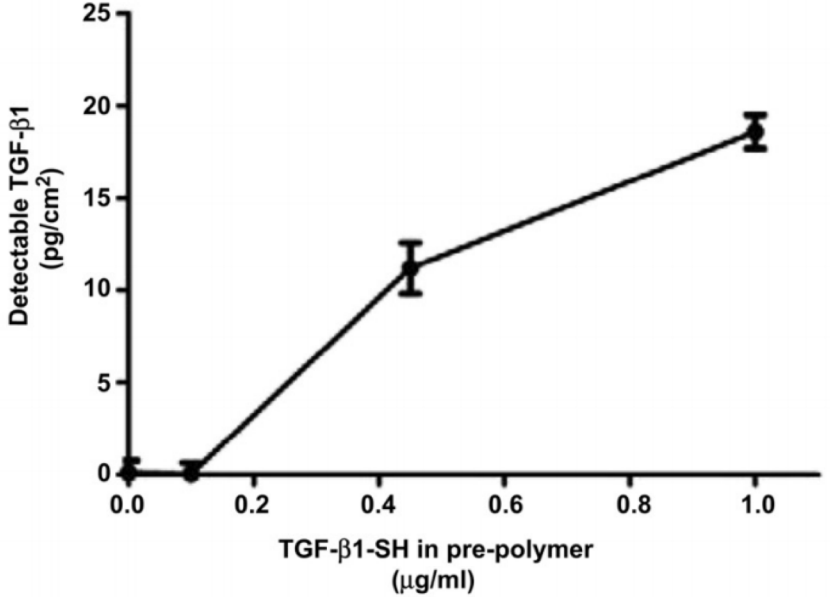
Strategy	Factor	*In vitro*	*In vivo*	Ref.
Material type	Decrease hydrophobicity	Decreased monocyte adhesion and FBGC formation	Decreased IL-6 and TNF-α production	45-47
	Remove cross-linking procedures		Increased M2 macrophage response	48
	Choice of common biomaterials	Reduced DC maturation or inflammatory cytokine production		49
		Non-adhesive substrates support IL-10 production		50
Surface topography	Aligned fibers		Reduced capsule thickness	51
	Creating microstructure	Reduced monocyte fusion and induced M1/M2 hybrid phenotype	Decreased capsule formation	52-54
Surface treatments	Increase hydrophilicity	Limited DC maturation		55
	Grafted microparticle hydrogels	Reduced protein adsorption and monocyte adhesion	Reduced leukocyte adhesion and inflammatory cytokine production	56
	Osteopontin coating		Reduced capsule thickness of positively charged polymer surfaces	57
	Surfactant polymer coating		Reduced fouling and platelet adhesion	58

Boehler et al. “Tissue engineering tools for modulation of the immune response” *BioTechniques* 51, (2011): 239-254.

Delivery of anti-inflammatory agents

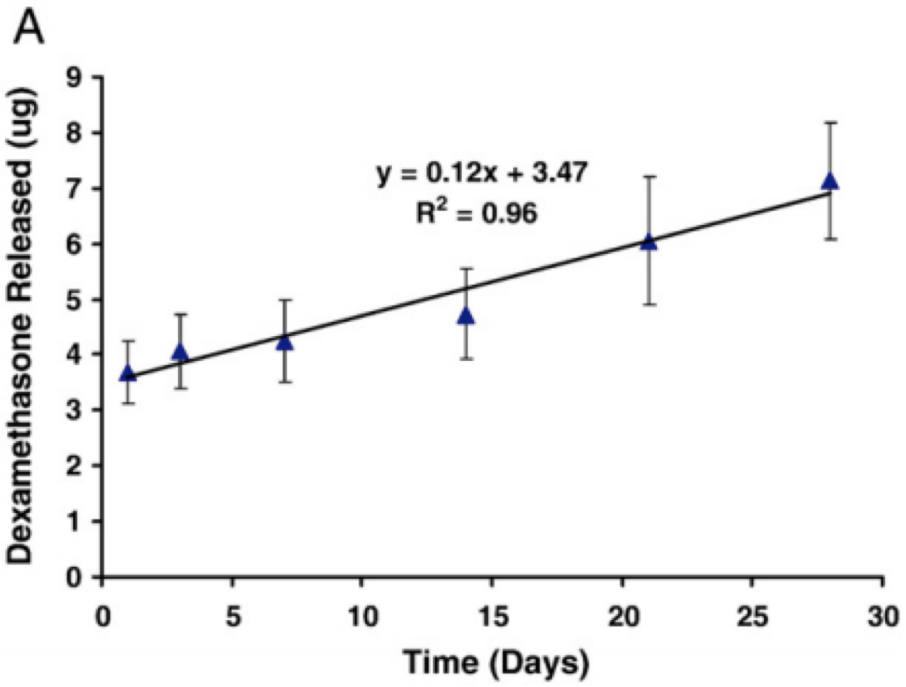
- PEG hydrogels immobilized with TGF-β and IL-10
- In presence of photoinitiator, PEGDA crosslinks and binds thiol groups on proteins in radical-mediated reaction
- General approach to modify biomaterial surfaces with any thiolated protein

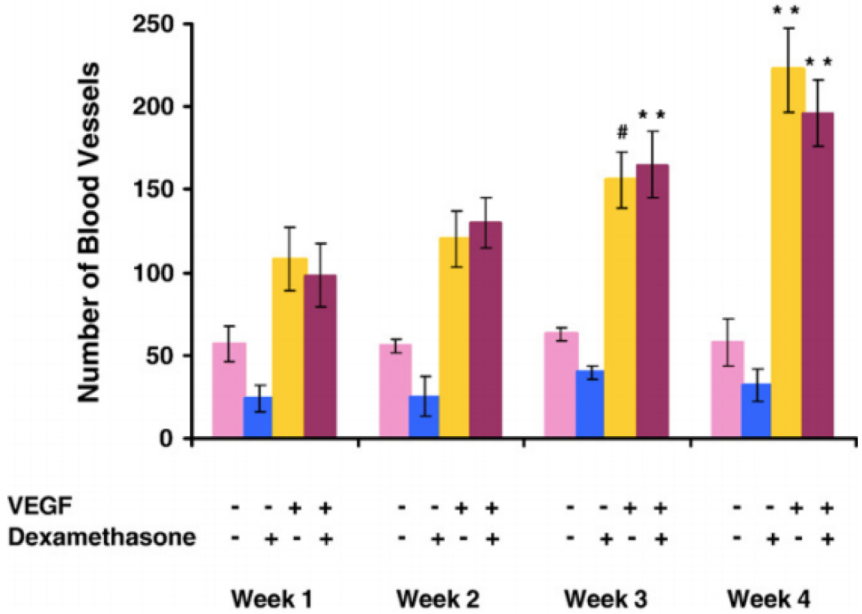




Hume et al. "Strategies to reduce dendritic cell activation through functional biomaterial design" *Biomaterials*, 33, (2012): 3615-3625.

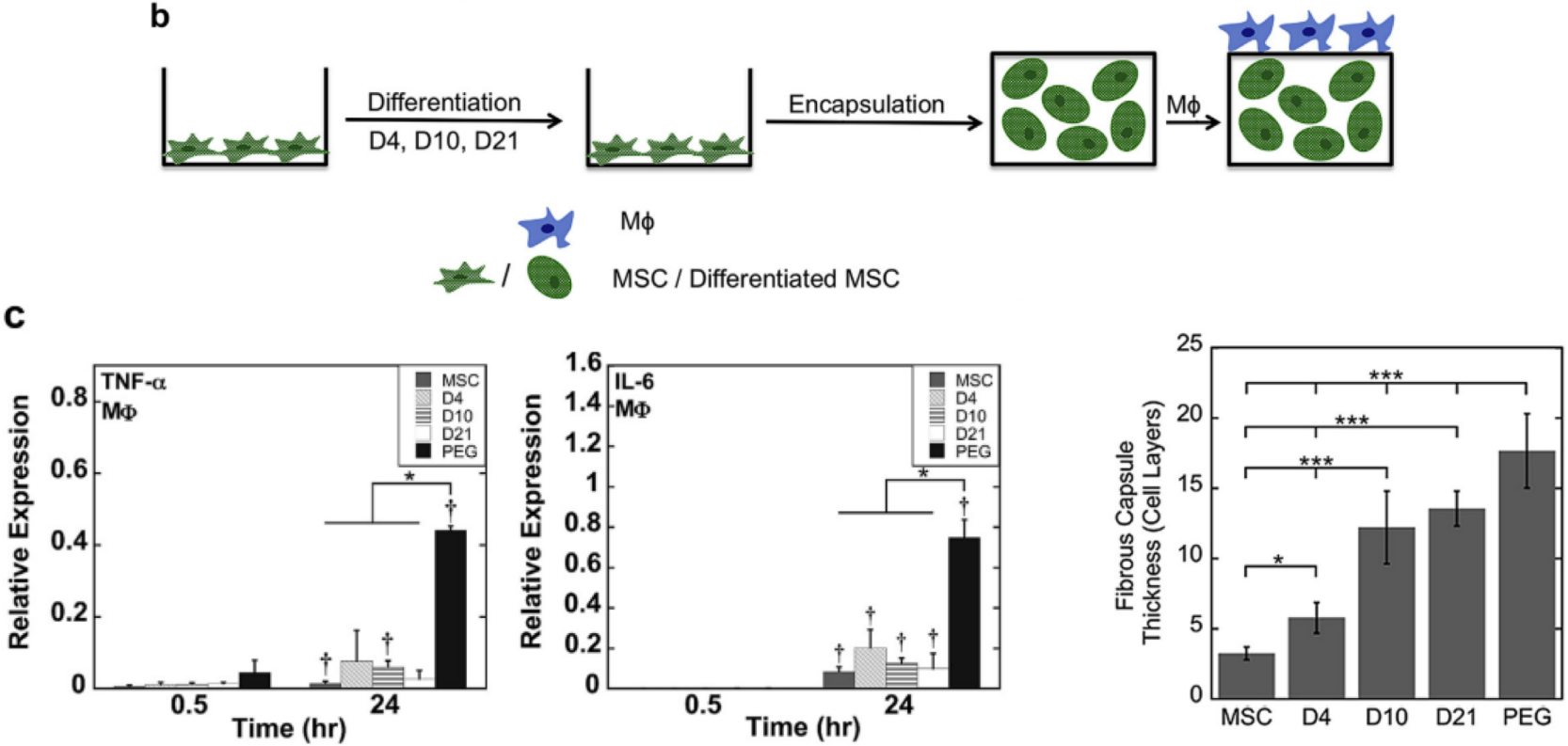
Delivery of anti-inflammatory agents





Patil et al. "Concurrent delivery of dexamethasone and VEGF for localized inflammation control and angiogenesis" *Journal of Controlled Release* 117, (2007): 68-79.

Cell-based strategies



Swartzlander et al. "Immunomodulation by mesenchymal stem cells combats the foreign body response to cell-laden synthetic hydrogels" *Biomaterials* 41, (2015); 79-88.