

Johns Hopkins Engineering

# Immunoengineering

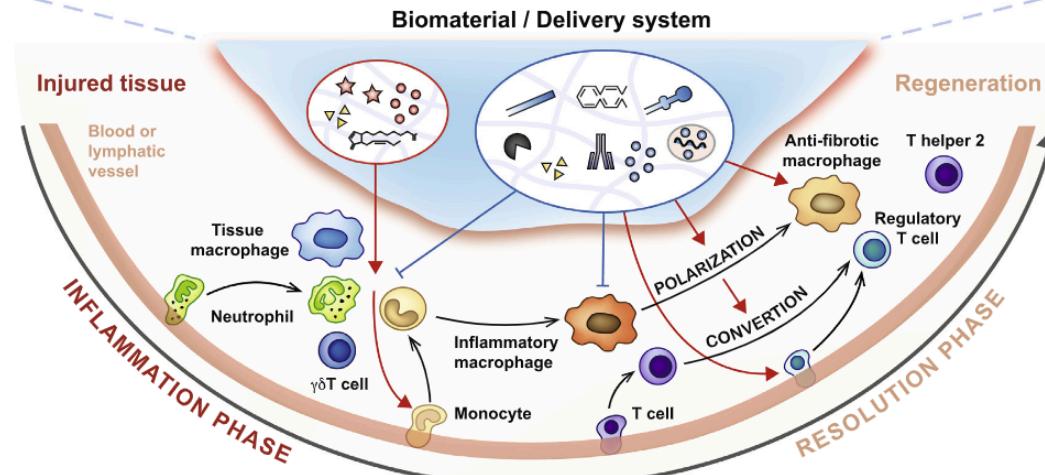
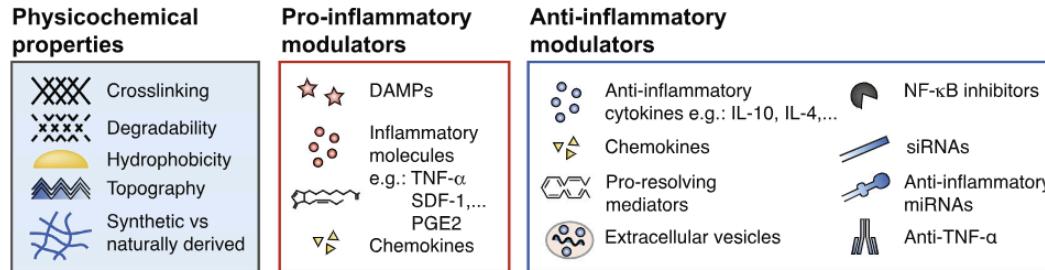
Immunoengineering: Tissue Engineering

Engineering Immunomodulatory Biomaterials for Tissue Engineering

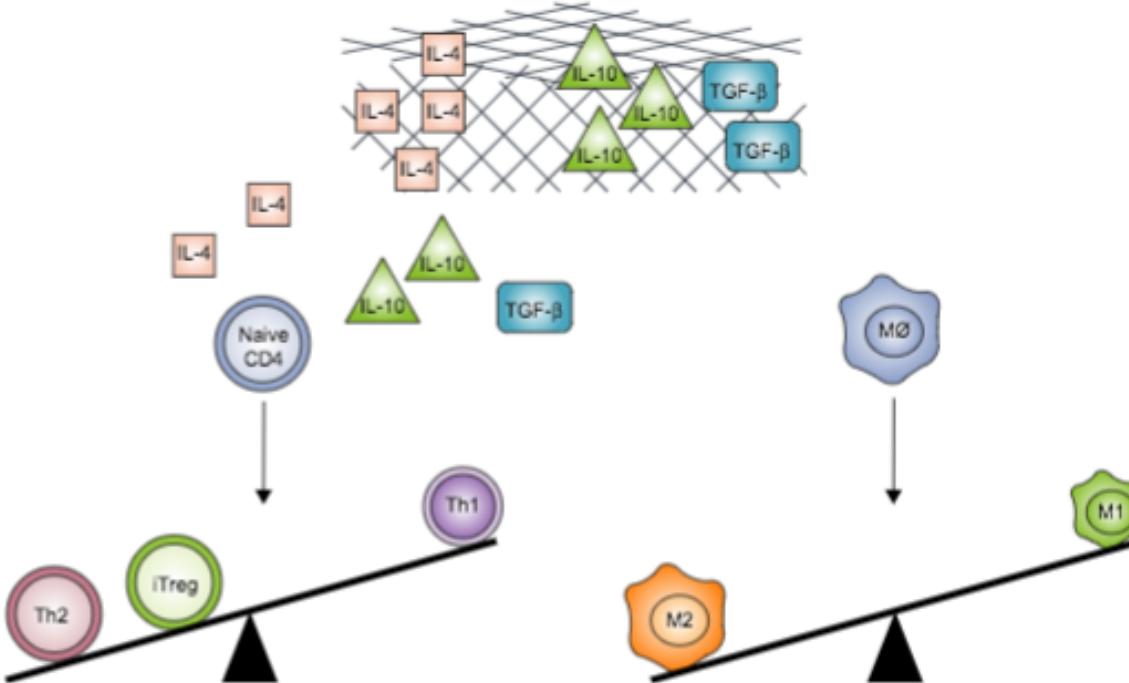


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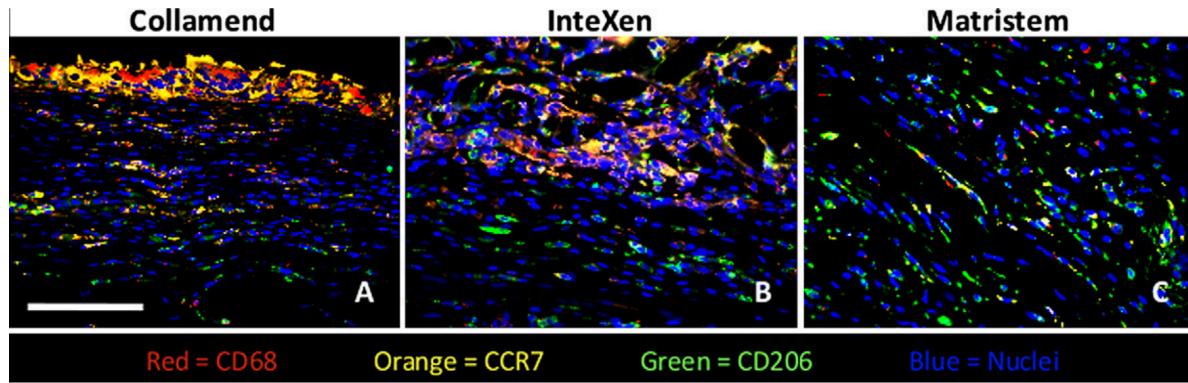
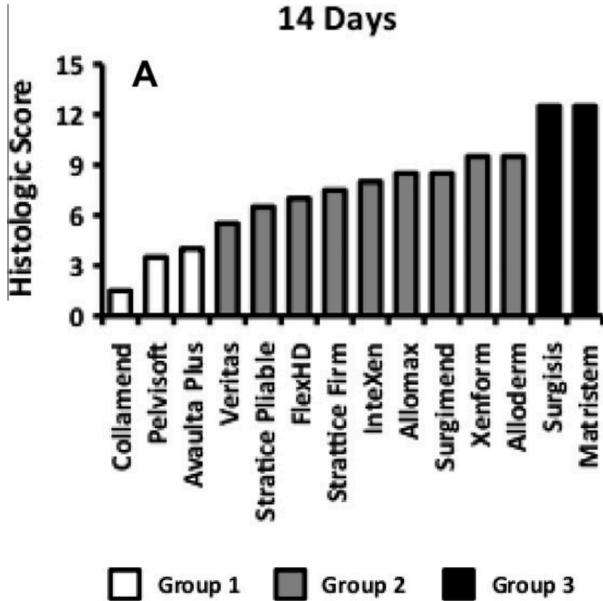
# Biomaterial Strategies for Immunomodulation to Promote Tissue Regeneration



# Modulating macrophage and T cell phenotypes

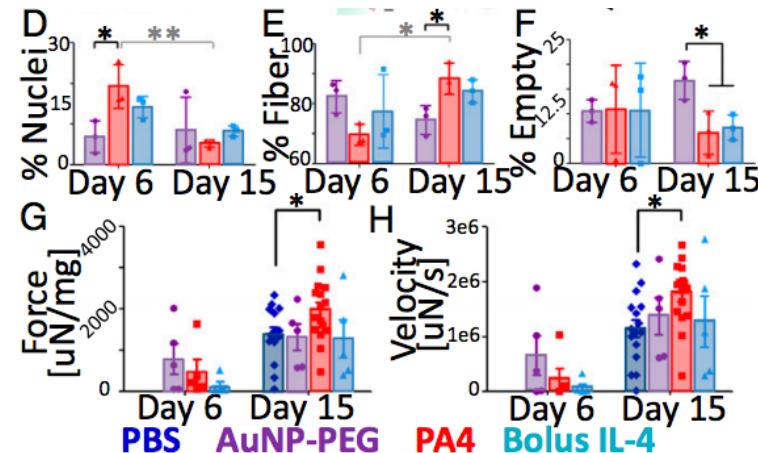
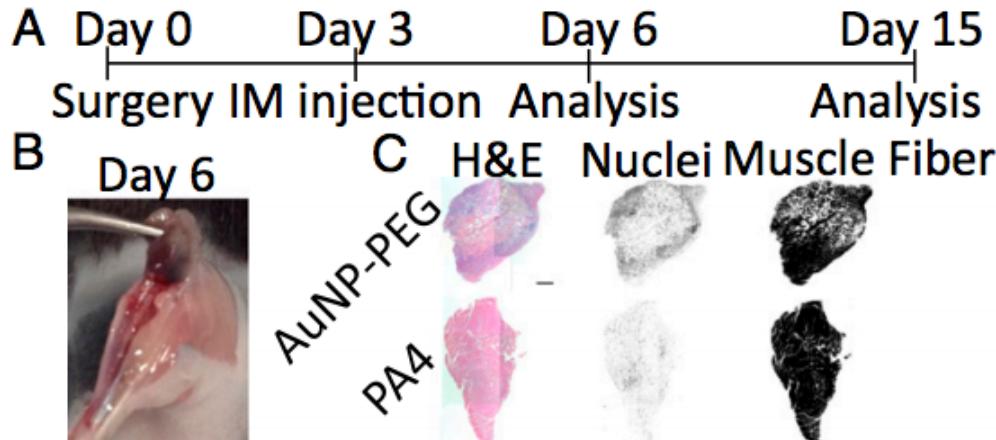
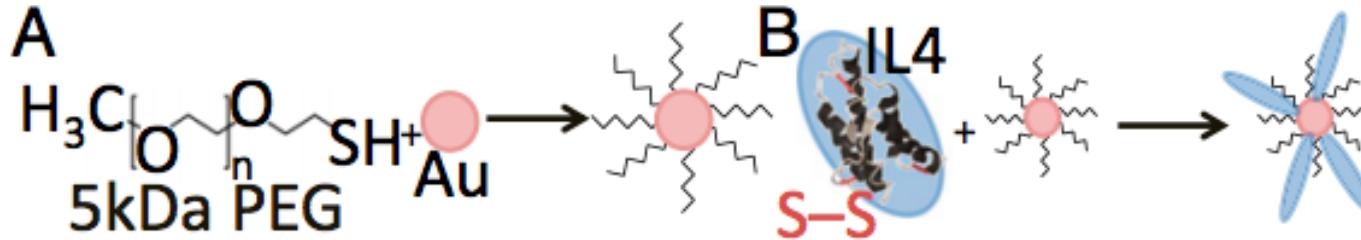


# Biomaterial influences macrophage phenotype and tissue remodeling response



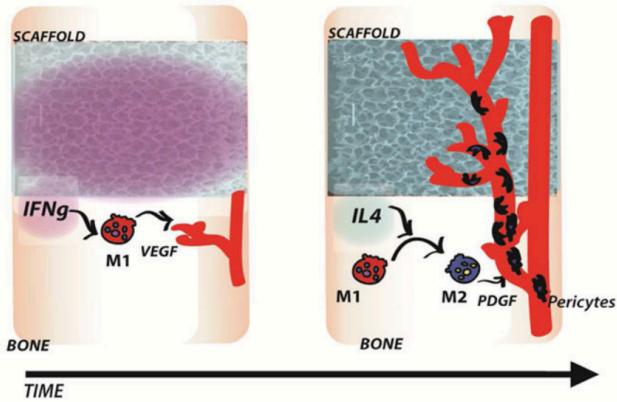
CD68- pan macrophage marker  
CCR7- M1 marker  
CD206- M2 marker

# Modulating macrophage polarization to M2 phenotype to enhance muscle regeneration



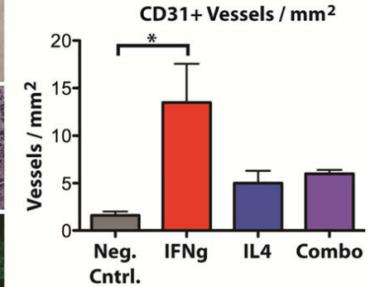
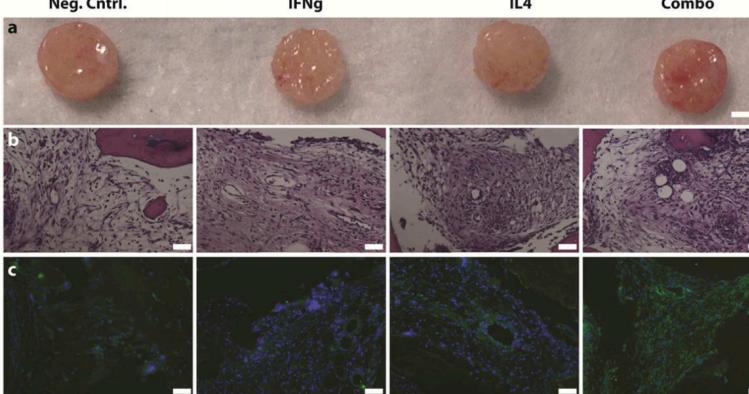
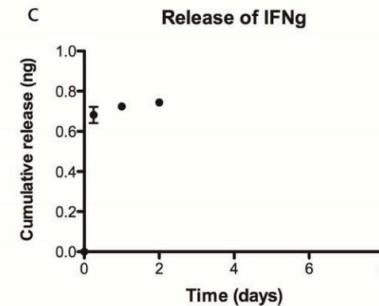
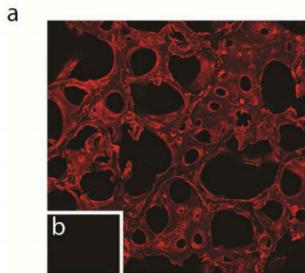
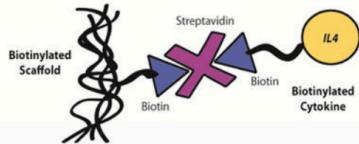
# Delivery of immunomodulatory cytokines to enhance vascularization of bone scaffolds via macrophages

## b Study 2: Ability of scaffolds to facilitate phenotypic switch



Groups: Negative Control (Neg. Cntrl.), Adsorbed IFN-gamma only (IFNg), Attached IL4 only (IL4), and their combination (Combo)

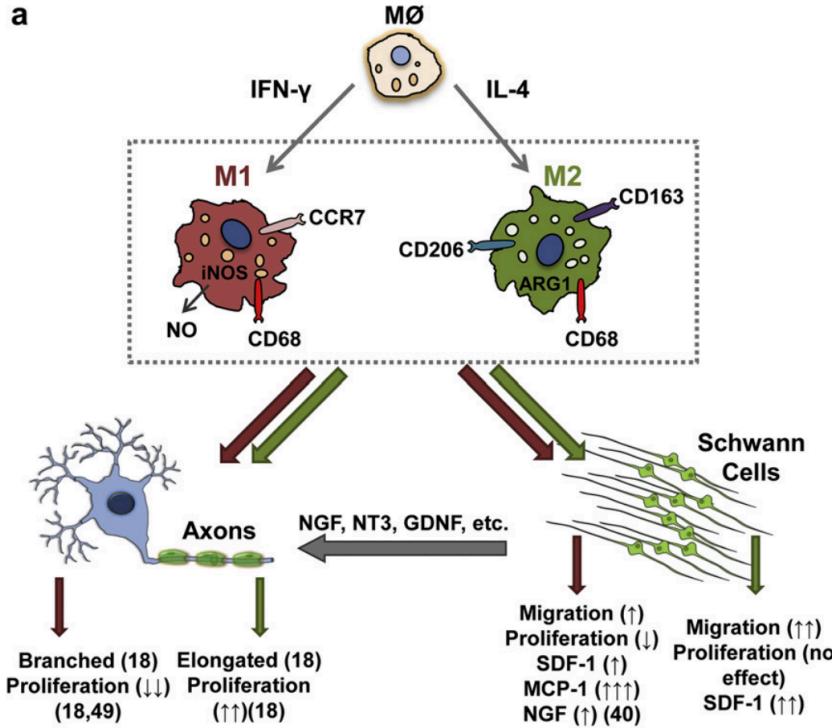
## c Method of attachment of IL4 to bone scaffolds



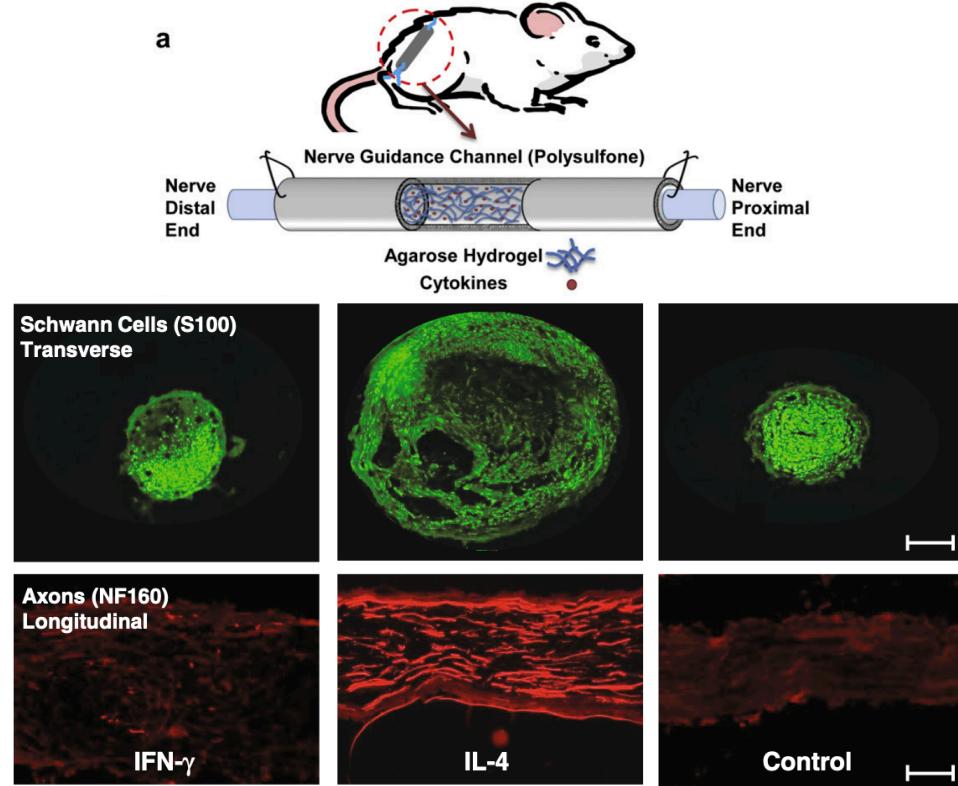
Spiller et al. "Sequential delivery of immunomodulatory cytokines to facilitate the M1-to-M2 transition of macrophages and enhance vascularization of bone scaffolds" *Biomaterials* 37, (2015): 194-207.

# Effect of macrophage modulation on nerve regeneration

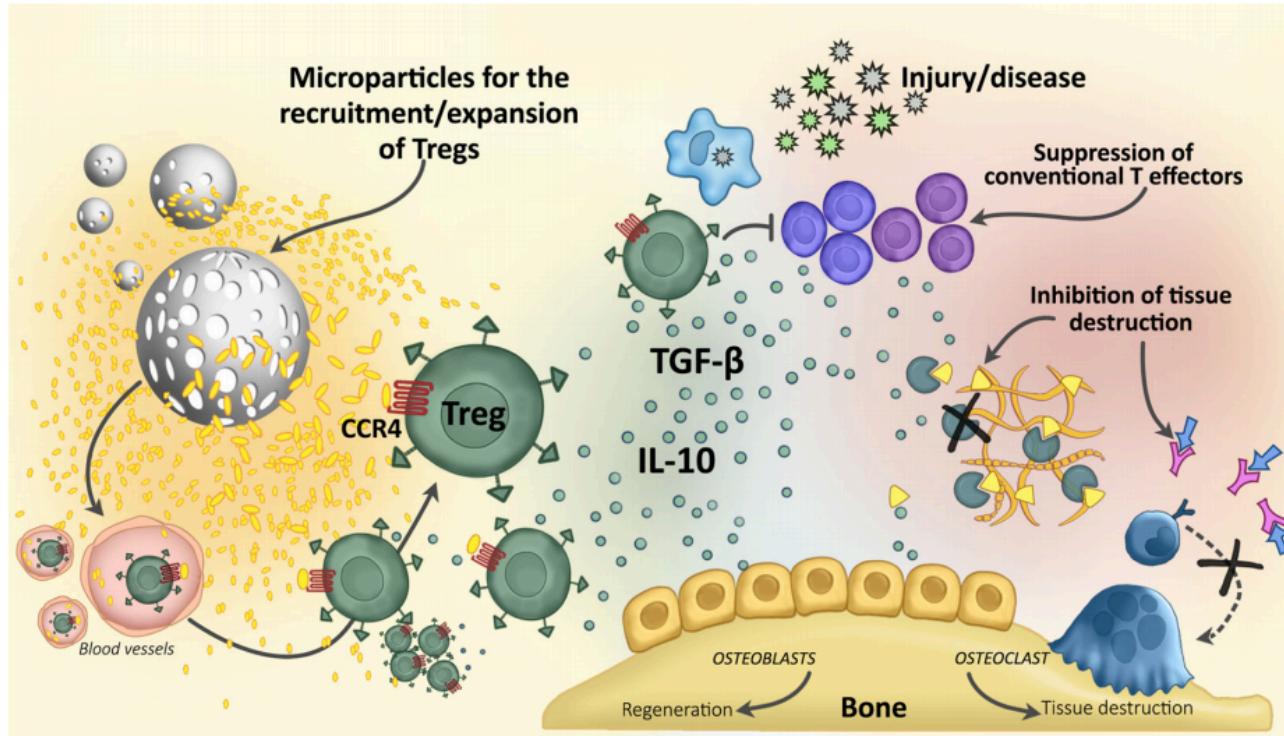
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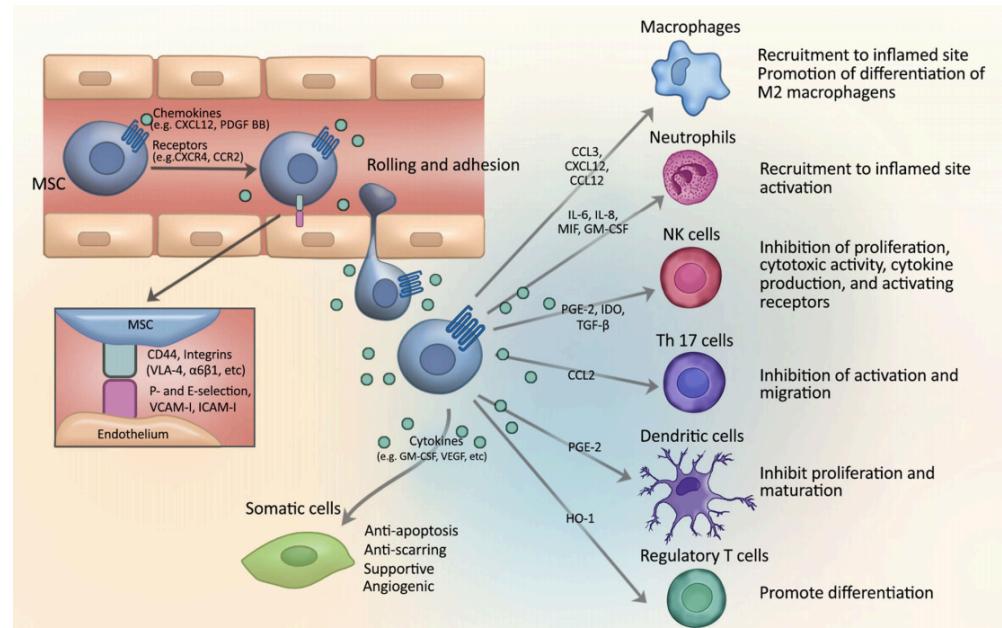
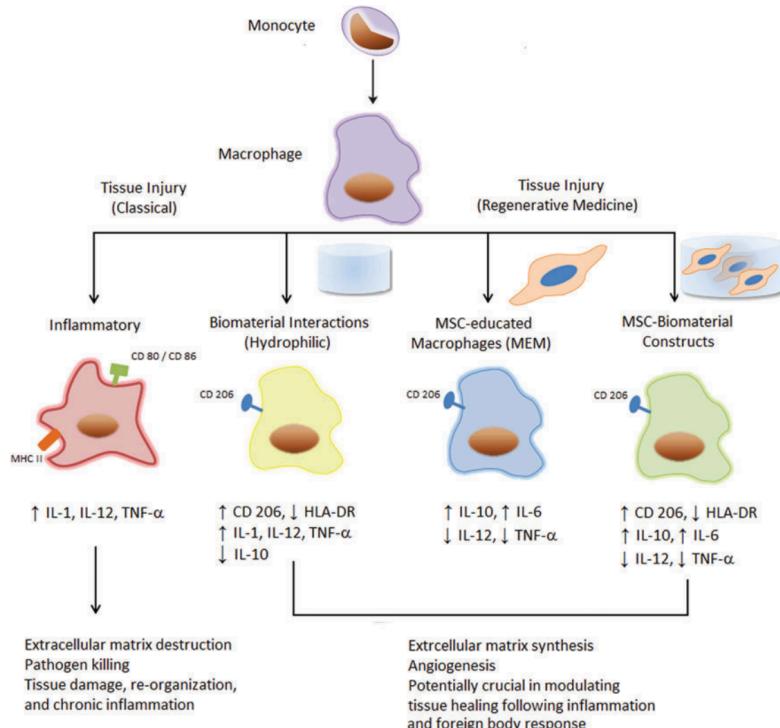


# Biomaterials to modulate T cell phenotype



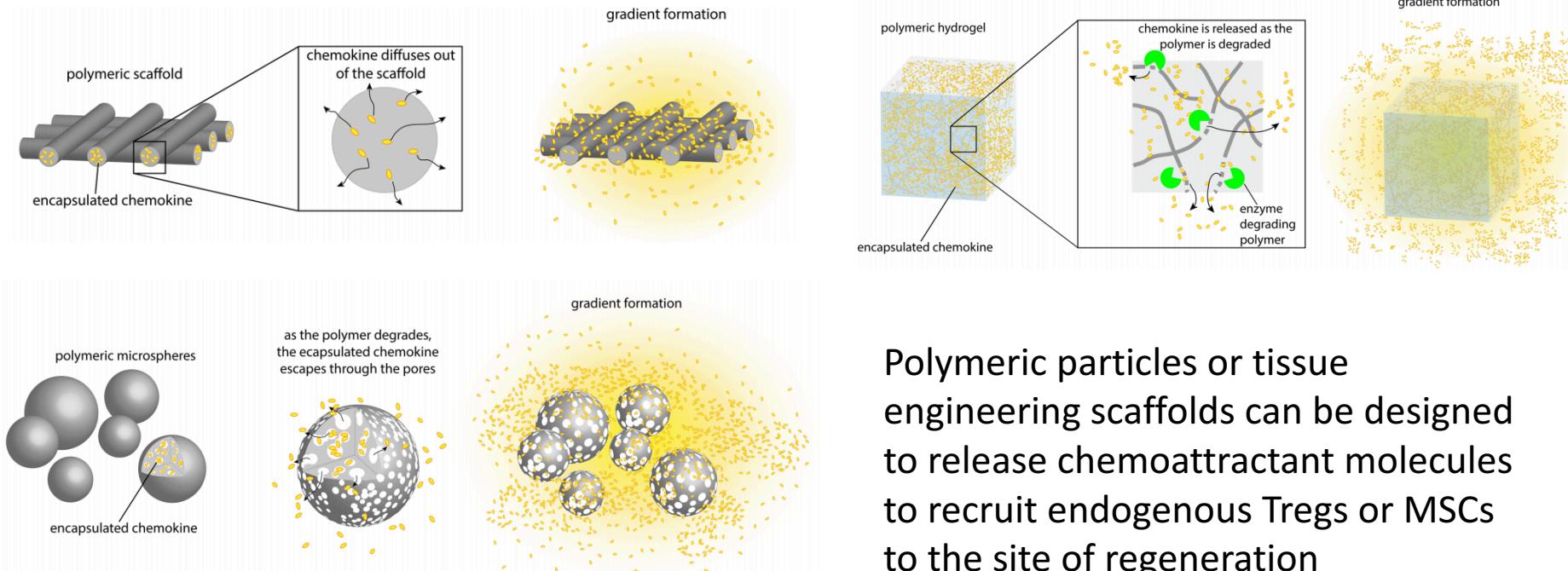
Glowacki et al. "Strategies to Direct the Enrichment, Expansion, and Recruitment of Regulatory Cells for the Treatment of Disease" *Annals of Biomedical Engineering* 43(4), (2015): 592-602.

# MSCs (Mesenchymal Stem Cells)



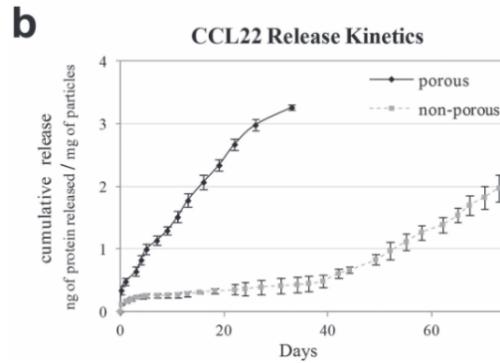
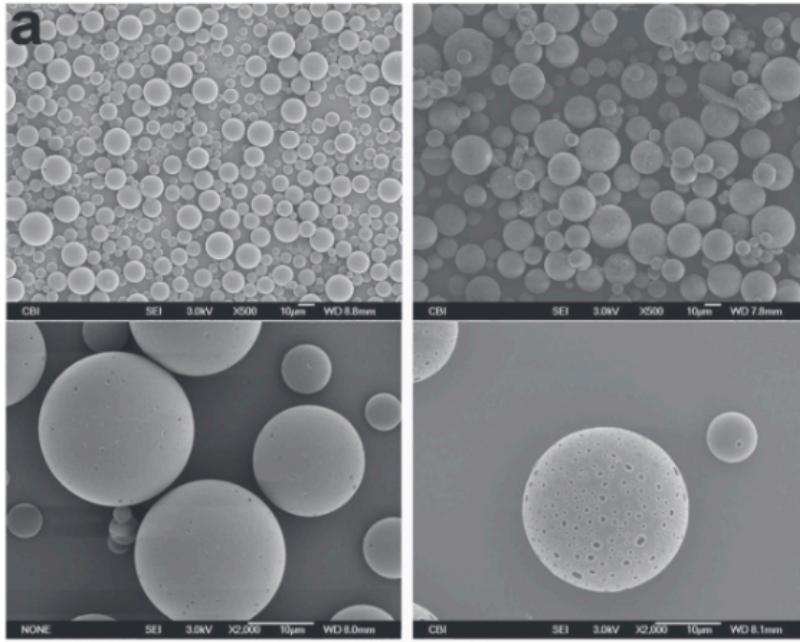
Hanson et al. "Biomaterial-Mesenchymal Stem Cell Constructs for Immunomodulation in Composite Tissue Engineering" *Tissue Engineering: Part A* 20(15-16), (2014): 2162-2168.; Glowacki et al. "Strategies to Direct the Enrichment, Expansion, and Recruitment of Regulatory Cells for the Treatment of Disease" *Annals of Biomedical Engineering* 43(4), (2015): 592-602.

# Engineering biomaterials to attract Tregs and/or MSCs

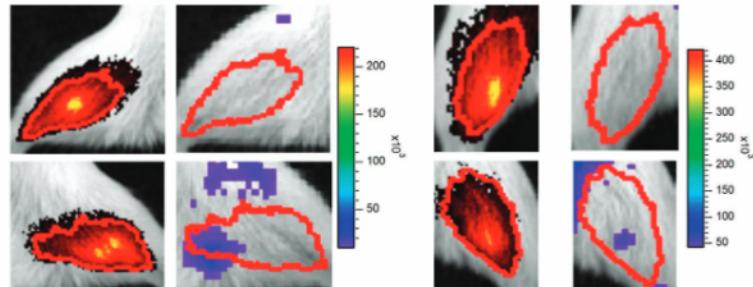


Polymeric particles or tissue engineering scaffolds can be designed to release chemoattractant molecules to recruit endogenous Tregs or MSCs to the site of regeneration

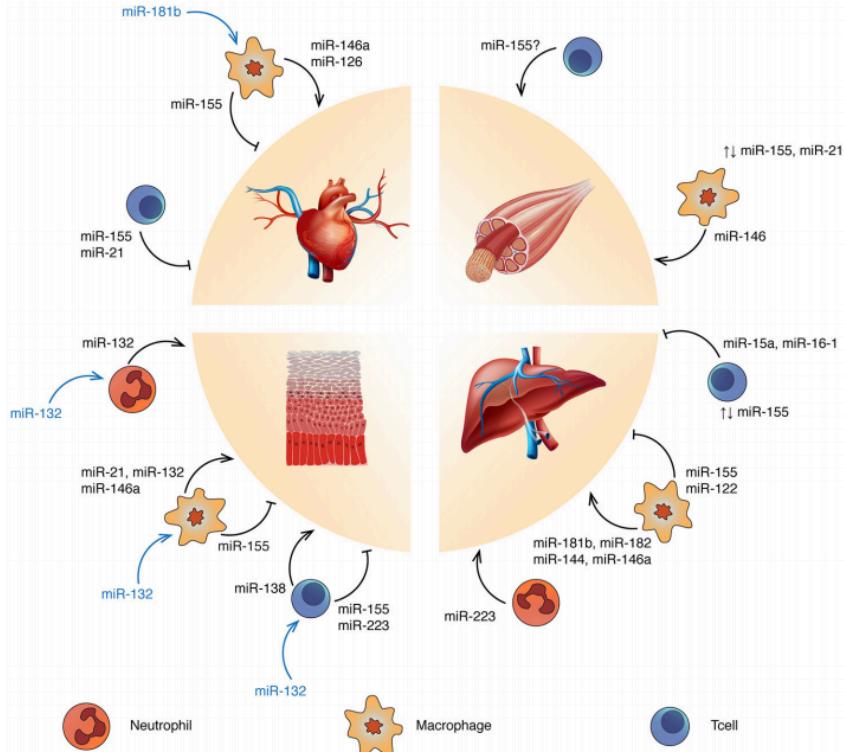
# CCL22-releasing PLGA microparticles to recruit Tregs



**a** Colocalization of Treg with CCL22MP



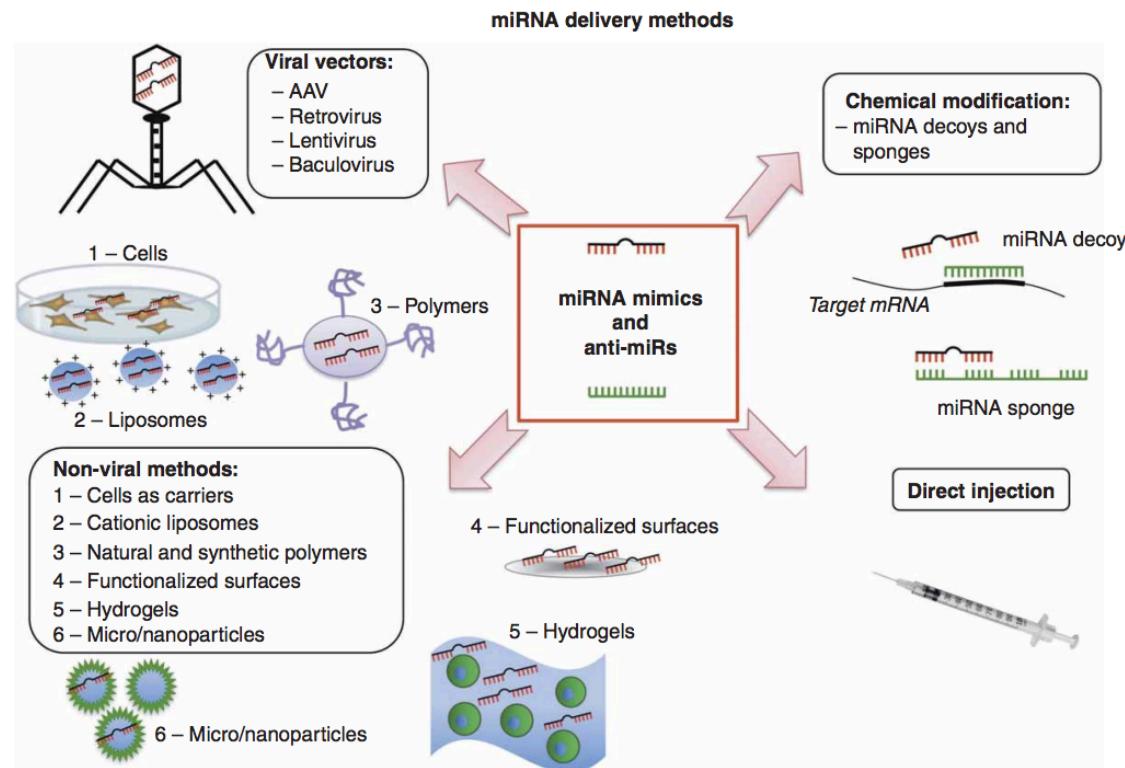
# Targeting immunoregulatory miRNAs for tissue regeneration



**Table 1A |** miRNA in pre-clinical and clinical trials for regenerative medicine.

Agent	Method of administration	Therapeutic effect	Clinical trial
<i>miR-29 mimics MRG-201</i>	Direct skin injection	Anti-fibrous scar formation	Phase I
<i>LNA-anti-miR-208 MGN-9103</i>	Intravenous injection	Treatment of chronic heart failure, preventing hypertrophy, fibrosis and pathological remodeling	Pre-clinical trial
<i>LNA-anti-miR-15 family MGN-1374</i>	Intravenous injection	Post-myocardial infarction remodeling, enhances cardiomyocytes proliferation	Pre-clinical trial
<i>2' Ome anti-miR-21 RG-012</i>	Subcutaneous injection	Alport syndrome, decreases renal fibrosis progression	Phase II
<i>2'MOE, 2' fluoro-sugar modified nucleosides anti-miR-155</i>	Intraperitoneal injection	Amyotrophic lateral sclerosis	Preclinical trial

# miRNA Delivery Strategies



Gori et al. "Tissue engineering and microRNAs: future perspectives in regenerative medicine" *Expert Opinion on Biological Therapy* 15(11), (2015): 1601-1622.



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