Development of Scaffolds for Regenerative Medicine by Molecular Imprinting

Nicholas A. Peppas^{1,2,3,4,5}

Departments of ¹Biomedical Engineering, ²Chemical Engineering, ³Surgery at the Dell Medical School, and ⁴Pharmacy ⁵Institute of Biomaterials, Drug Delivery, and Regenerative Medicine

The University of Texas at Austin, Austin, TX



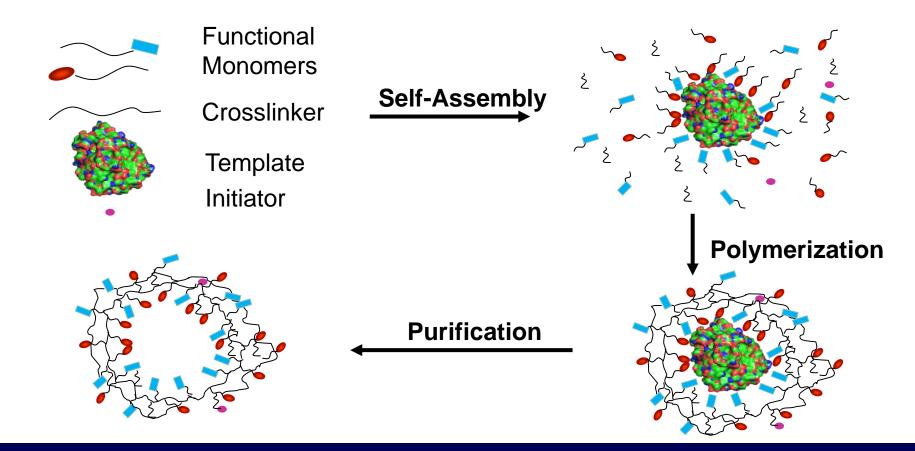




BIOMATERIALS, DRUG DELIVERY & REGENERATIVE MEDICINE

SUMMARY OF UNIVERSITY OF TEXAS PROJECT WITH THE UNIVERSITIES OF MINHO AND PORTO ACCOMPLISHMENTS / OUTCOMES

PREPARATION OF RECOGNITIVE SCAFFOLDS

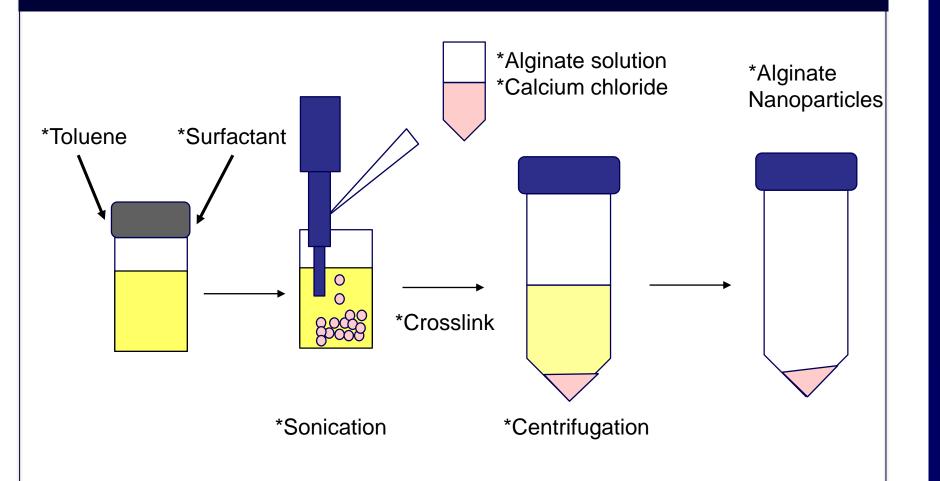


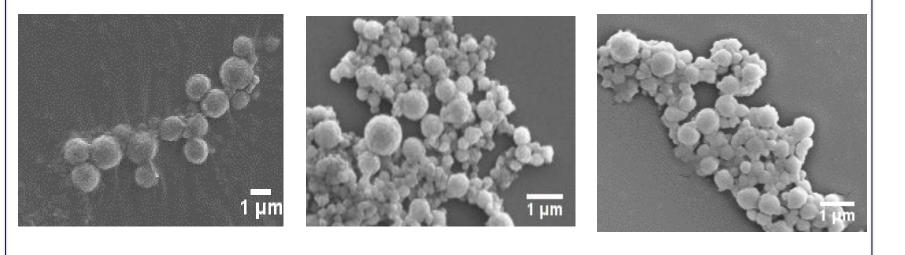
SIX SPECIFIC AIMS:

- 1) Synthesis of novel imprinted synthetic polymer hydrogels
- 2) Synthesis of novel imprinted natural-based polymer hydrogels
- 3) Quantitative characterization and binding of imprinted polymers
- 4) Incorporation of a degradable crosslinker into the polymer backbone
- 5) Assessment of the in vitro behavior of imprinted polymeric systems 6) Cellular adhesion, proliferation and growth on imprinted polymer gel scaffolds

SYNTHESIS OF NOVEL IMPRINTED SYNTHETIC POLYMER HYDROGELS Solvent displacement Polycaprolactone Evaporate (in acetone) acetone PMAO-g-PEGMA in water APS TEMED 30 min Template preassembly 16 4x Swell 0.1x PBS Initiation Purge Dialysis Collapse pH 7.4 buffer Cycles

SYNTHESIS OF NOVEL IMPRINTED NATURAL-BASED POLYMER HYDROGELS

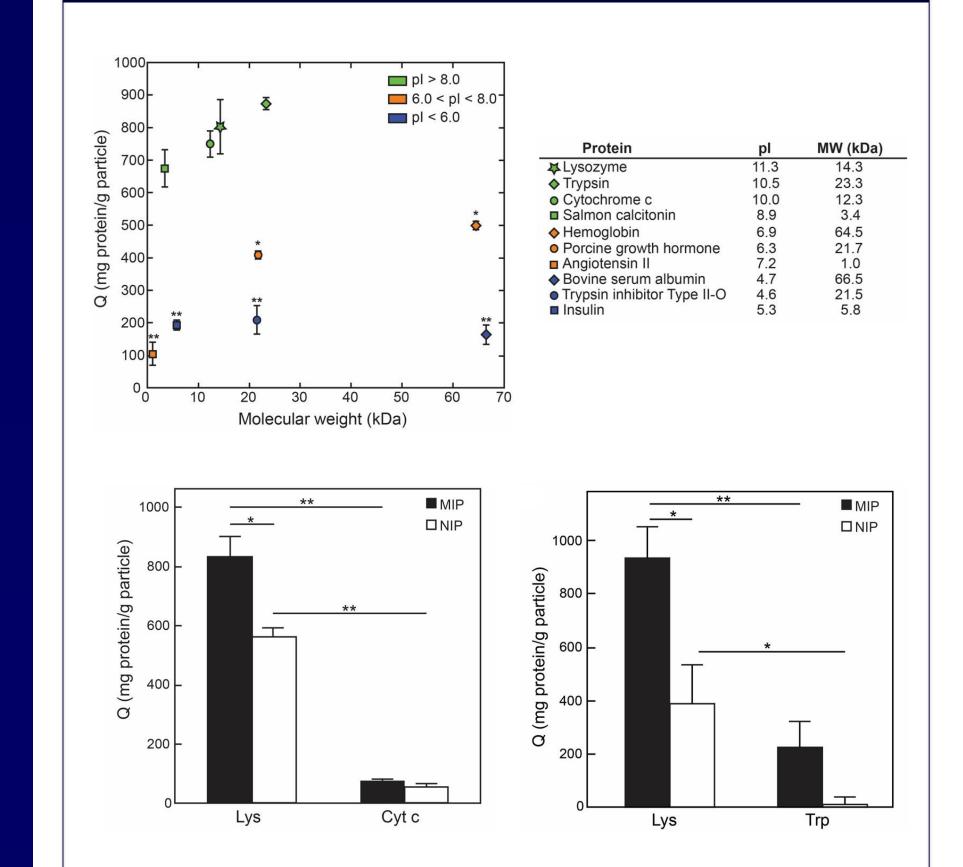




*0.5 % Alginate

*2% Alginate *1 % Alginate

QUANTITATIVE CHARACTERIZATION AND BINDING OF IMPRINTED POLYMER SCAFFOLDS



Achievements Goal 1:

- Synthesized, purified, and characterized new hydrogel nanoparticles
- Developed new molecularly recognitive • polymeric systems
- Imprinted protein templates in polymeric matrices

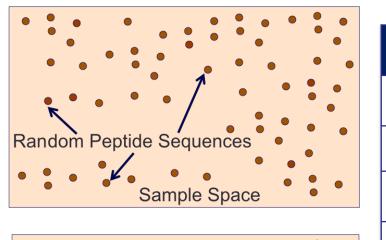
Achievements Goal 2:

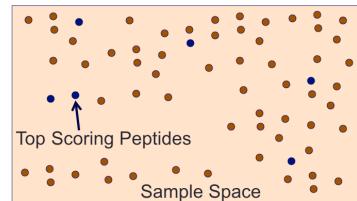
- Synthesized alginate-based recognitive matrices with protein therapeutics
- Fabricated alginate-based nanoparticle systems

Achievements Goal 3:

- Evaluated recognition and binding capacities of lysozyme imprinted scaffolds
- Characterized selectivity of imprinted particle systems in competitive environments
- Quantified binding capacities of lysozyme, and trypsin imprinted nanoparticles with similar proteins

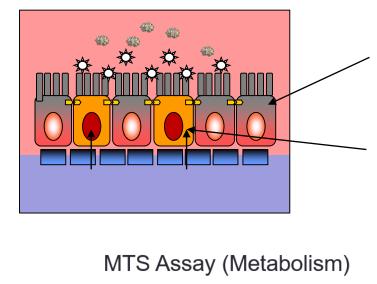
INCORPORATION OF PEPTIDES INTO THE POLYMER BACKBONE





ISOLATED SEQUENCES (EXTRACTED HIGHLIGHTED)			
ADCFLQ (88.45)	CDLWQY	FADWEC	LSCFLQ
ASCFLY	CDMWQY	CAHWAC	MNQCDY
CDAWQY	CDQWQY	FAHWWC (97.71)	MWQEMC
CDCWQY	CDNWQY (95.01)	FSCFLQ	NAHWEC
CDEWQY	CDWWQY	HAHWEC (95.27)	PECFMQ (85.90)
CDFWQY	CDQWQY	MAHWEC	QSCFLQ
CDHFAI (84.14)	CDQWQY	HSCFLQ	VAHWEC

ASSESSMENT OF THE IN VITRO BEHAVIOR OF IMPRINTED POLYMERIC SYSTEMS



Mean ± SEM, n=6

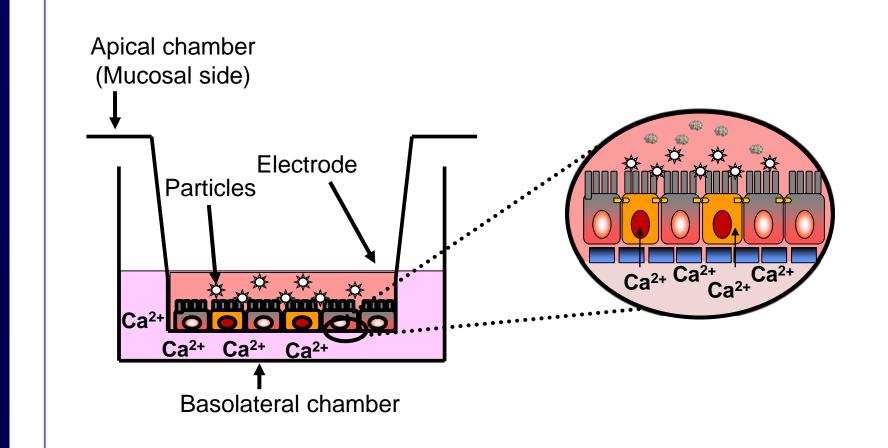
aco

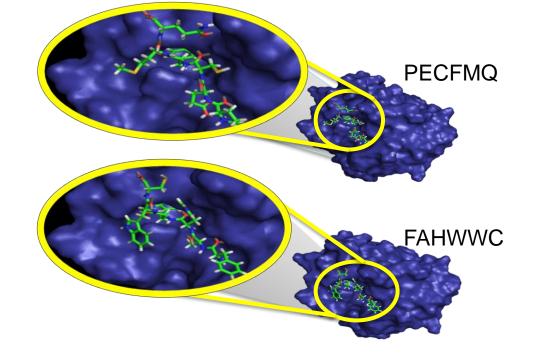
Human epithelial colorectal Caco-2: adenocarcinoma cells

HT29-MTX: Mucus-secreting intestinal cells

LDH Assay (Membrane Integrity) Mean ± SEM, n=3 ■ MIPs ■ NIPs

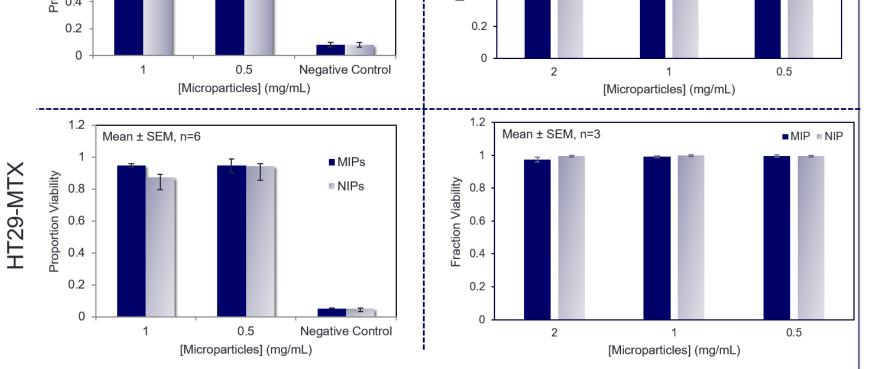
CELLULAR ADHESION, PROLIFERATION AND **GROWTH ON IMPRINTED POLYMER GEL** SCAFFOLDS





Achievements Goal 4:

- Generated and selected peptide sequences that interact most strongly with trypsin protein using molecular simulations
- Incorporated oligopeptides into polymeric systems
- Evaluated the recognitive ability of peptidetargeted polymeric nanoparticles



Achievements Goal 5:

- Established an intestinal cell-mimicking model using Caco-2 and HT29-MTX coculture
- Evaluated the cytotoxicity of molecularlyimprinted polymeric particles

Goals for Aim 6:

Evaluate the ability of molecular imprinted deliver systems to protein polymer therapeutics in an intestinal in vitro model

ACKNOWLEDGMENTS

The authors acknowledge Dr. Manuela Gomes and Dr. Rui Reis (University of Minho), and Dr. Pedro Granja (University of Porto). We also acknowledge the funding from the UT-Portugal CoLab program.