

# **Bian Lab**



The Chinese University of Hong Kong  
香港中文大學

## **Biomaterials & Stem Cell Tissue Engineering Laboratory**

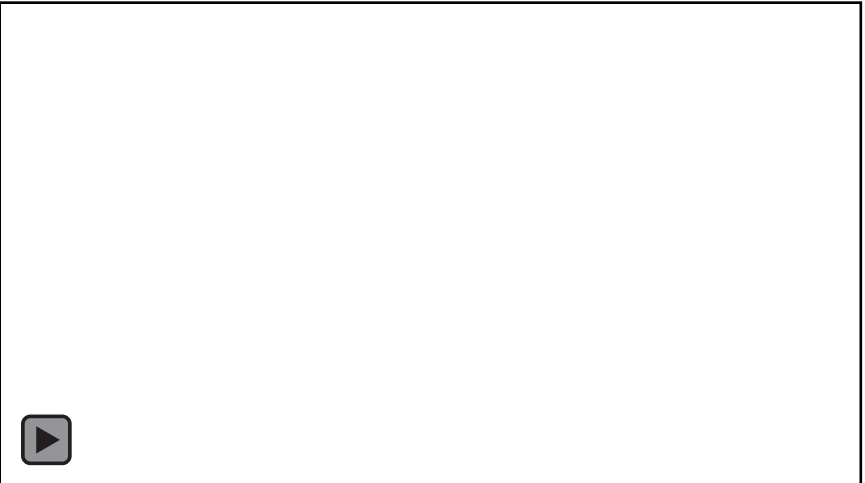
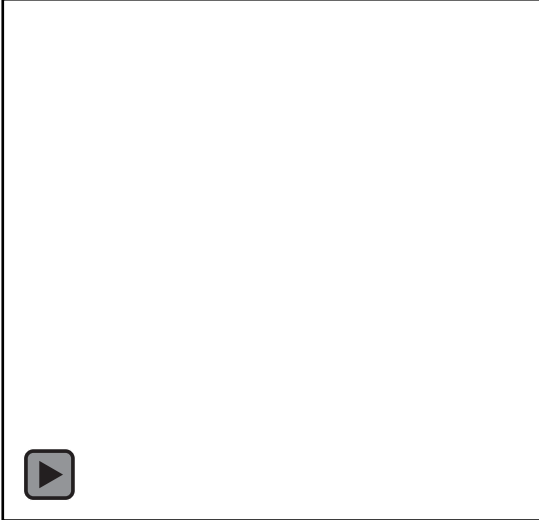
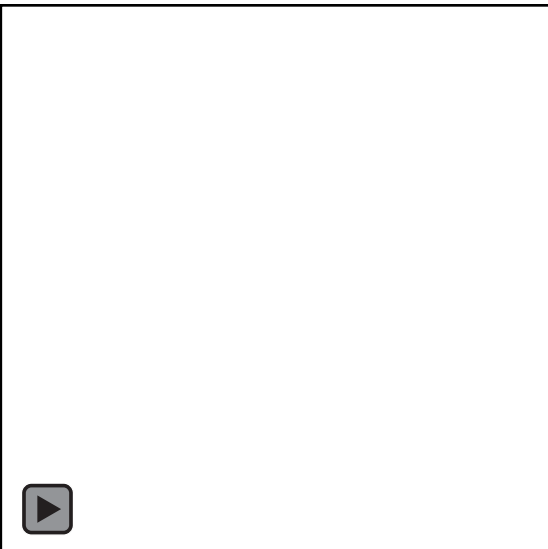
**Engineering molecular dynamics of polymeric biomaterials for  
fundamental and translational research**

**Bian Liming, 边黎明**

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Wechat:bianliming12**

**Biomedical Engineering Division  
The Department of Mechanical and Automation Engineering  
The Chinese University of Hong Kong**

# Molecular dynamics in polymeric materials inside and outside the cells



## Current research theme:

# Engineering functional biomaterials for regenerative medicine

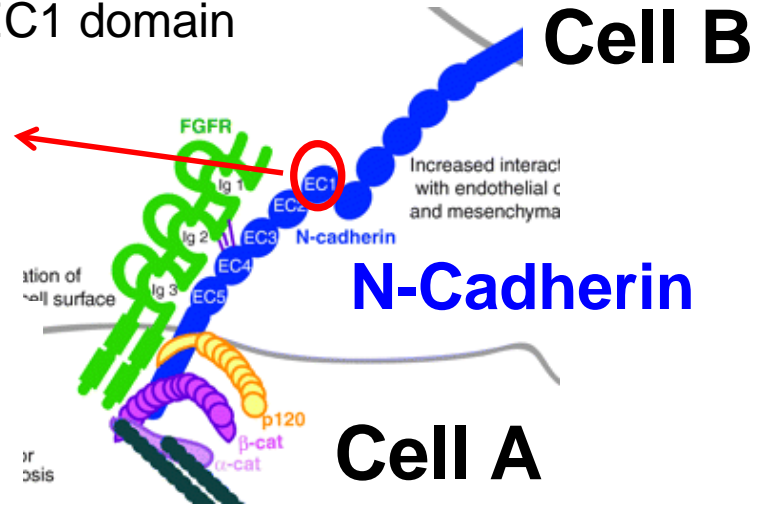
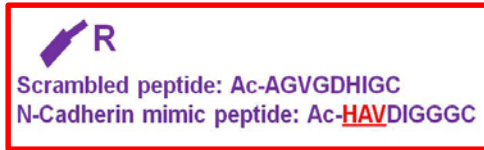
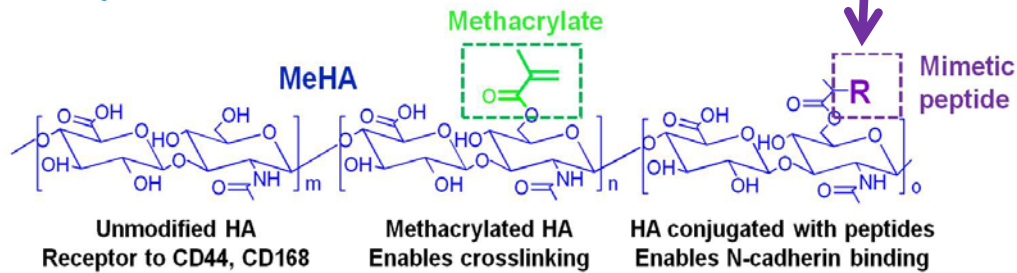
- Developmentally biomimetic materials: temporal and spatially-dynamic presentation of development-relevant cues to stem cells
  - PNAS, 2013
  - Biomaterials, 2012, 2016, 2017, 2018
  - Acta Biomater., 2014, 2017
  - JBMR-B, 2016
- **Dynamic hydrogels: incorporating network dynamics to** boosting bulk properties and regulate cell behaviors in 3D
  - Macromolecules, 2016
  - Biomaterials, 2016
  - Acta Biomater., 2016
  - Adv. Funct. Mater., 2017
  - Biomaterials Science, 2017
  - Chem. Mater., 2017
  - NPG Asia Mat., 2017, 2018
- **Dynamic nanostructures:** regulating nanoscale presentation of bioactive ligands to stem cells and immune cells
  - J. Am. Chem. Soc., 2015, 2018
  - Nano Letters, 2015, 2017, 2017
  - Adv. Funct. Mater., 2016
  - Adv. Healthcare Mater., 2016
  - Biomaterials, 2016, 2018
  - ACS Appl. Mater. Interfaces, 2017
  - ACS Nano, 2017, 2018
  - Small 2017

# Biofunctionalization of HA hydrogels with N-cadherin mimetic peptides

The HAV (Histidine Alanine Valine) sequence in EC1 domain plays a key role in N-cadherin binding

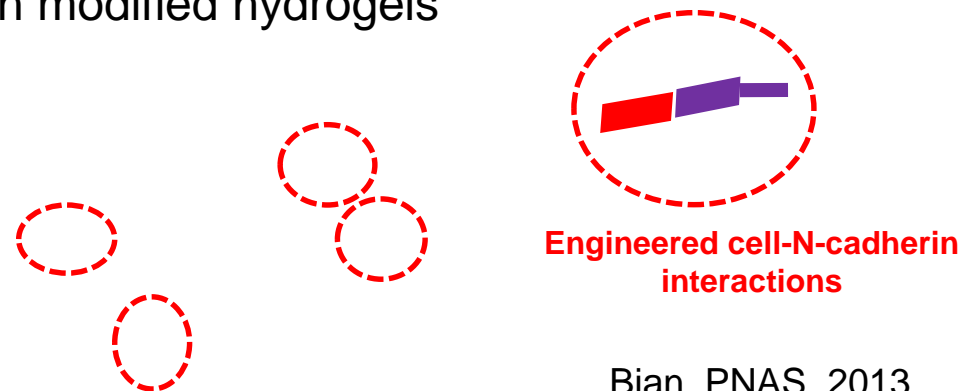


Conjugation to HA monomer via Michael-Type addition



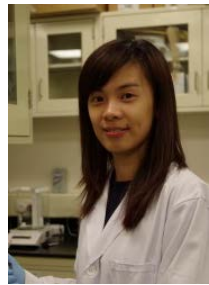
Margaret, 2007; Tuan 2002; Williams, 2002

Encapsulation of MSCs in N-cadherin modified hydrogels

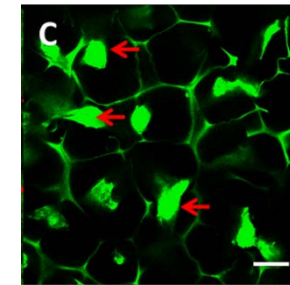
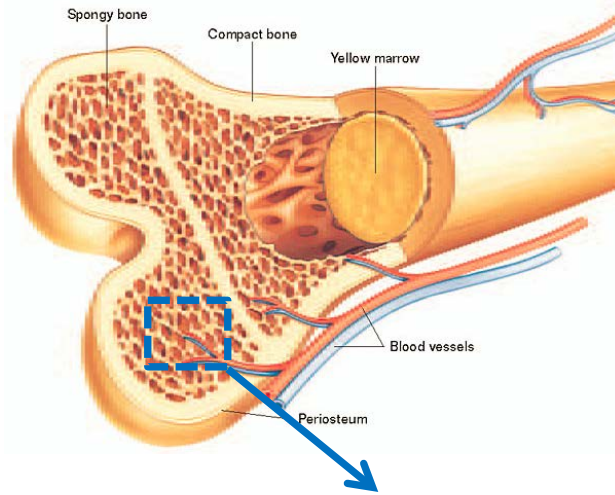


Bian, PNAS, 2013

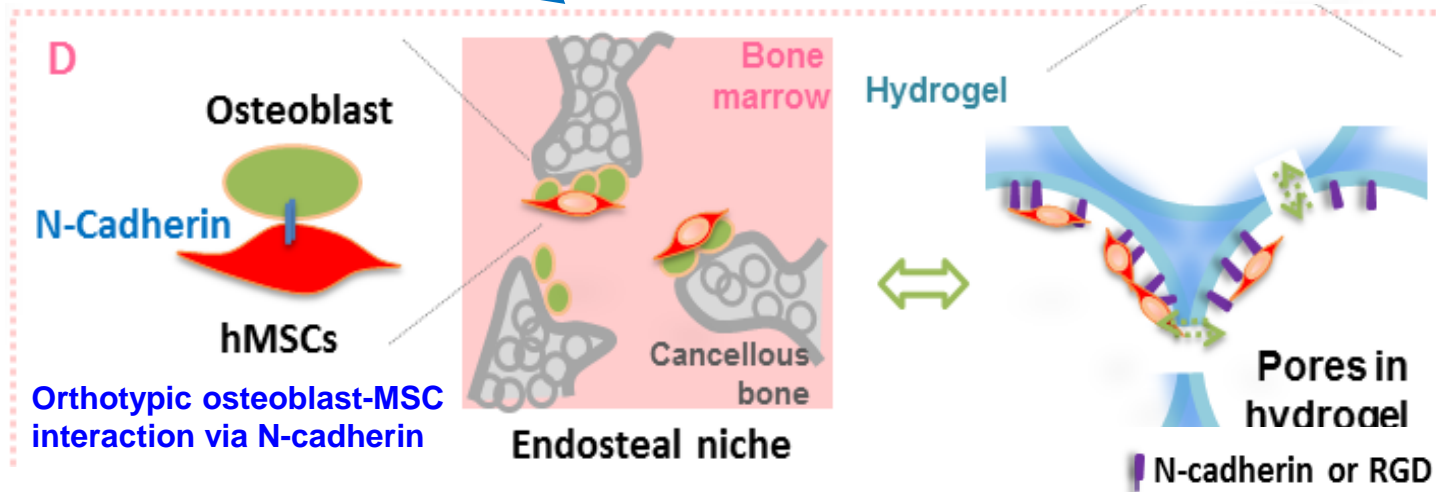
# N-Cadherin Mimetic Peptide Conjugated Hyaluronic acid (HA) hydrogels to emulate the pro-osteogenic endosteal niche



Zhu Meiling

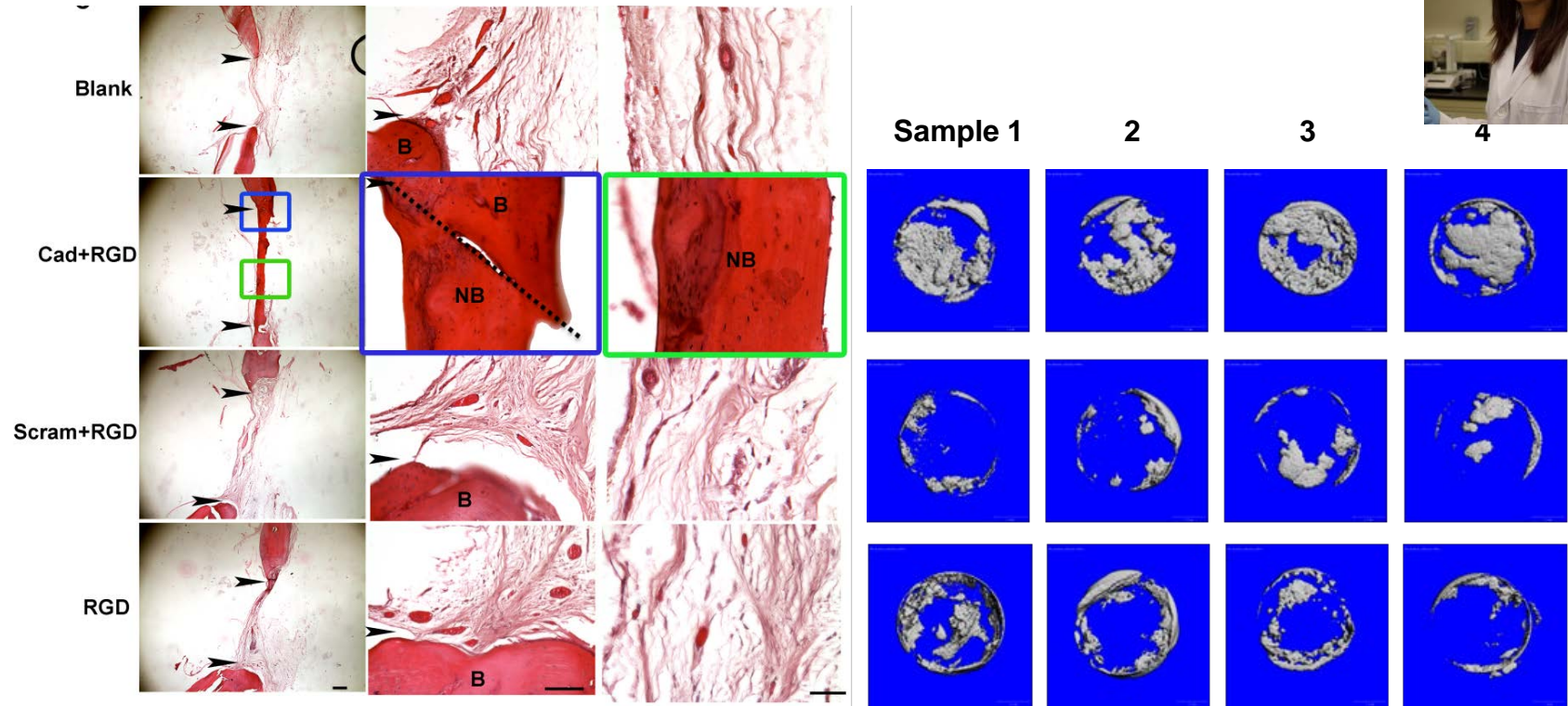
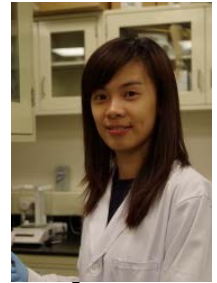


Arrow: stem cell



# N-cadherin peptide functionalized porous HA hydrogels promote rMSC osteogenesis in rat calvarial bone defect

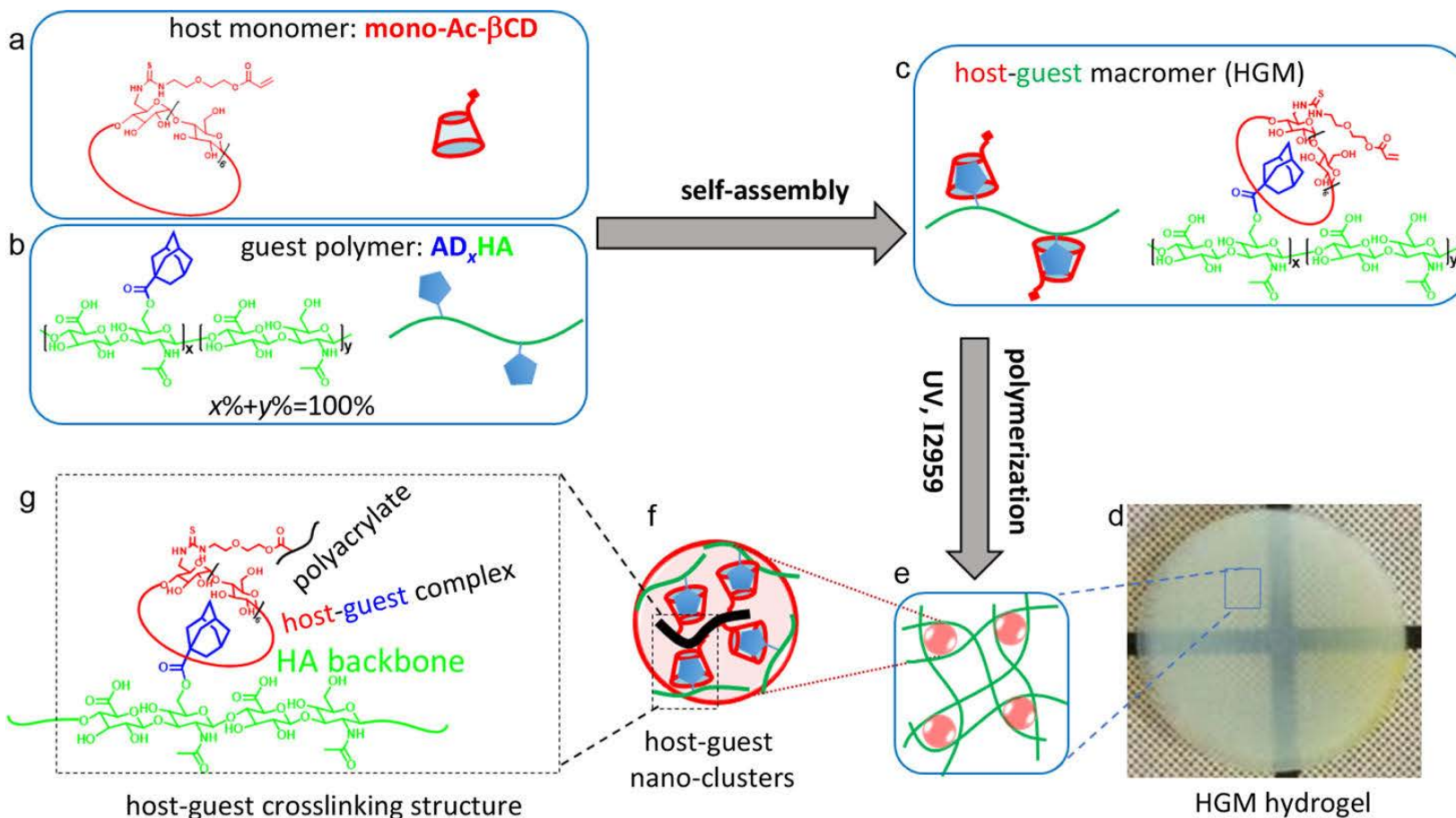
## H&E and microCT (12 weeks post implantation)



**Hydrogels decorated with cadherin peptide promote the osteogenesis of rMSCs at an orthotropic site in rats.**



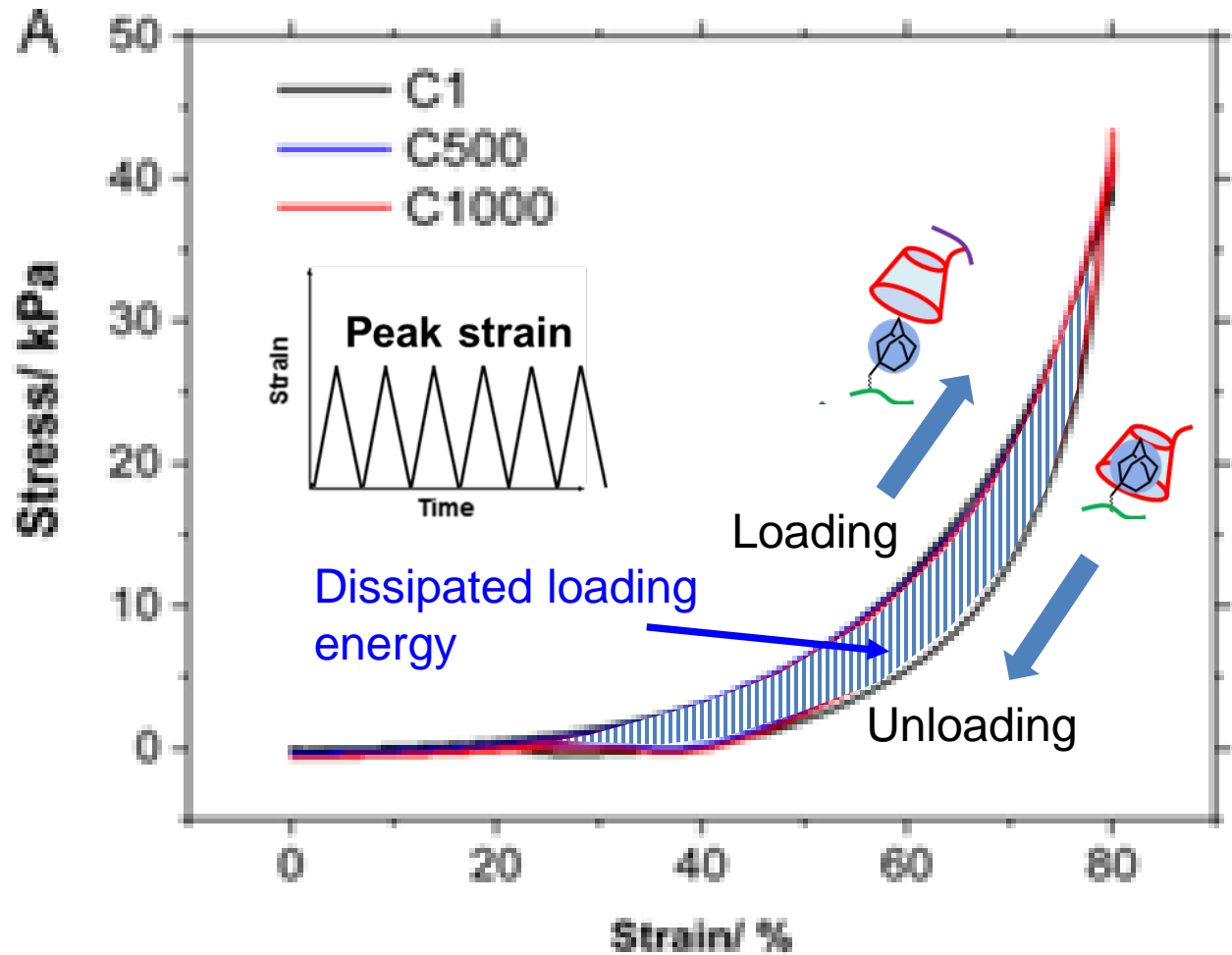
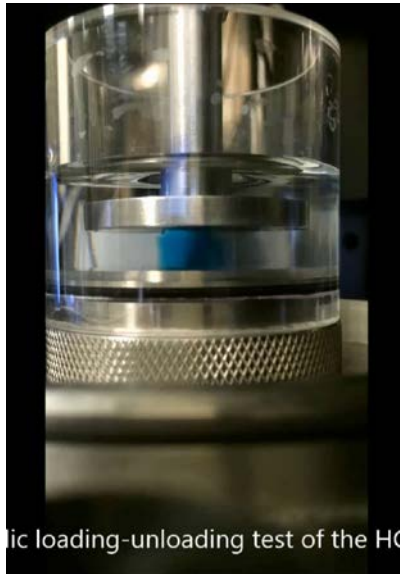
# Host guest macromer (HGM) supramolecular hyaluronic acid (HA) hydrogels



**Mono-ac- $\beta$ CD**: mono-acrylated beta-cyclodextrin (host monomer)

**AD<sub>x</sub>HA**: adamantane grafted on  $x\%$  of hyaluronic acid repeat units (guest-polymer)

# 2<sup>nd</sup> generation robust hydrogels: fatigue resistant HGM HA hydrogels



Dissipation of massive loading energy by the reversible physical crosslinking of the hydrogels



# Our supramolecular hydrogels possess robust mechanical properties

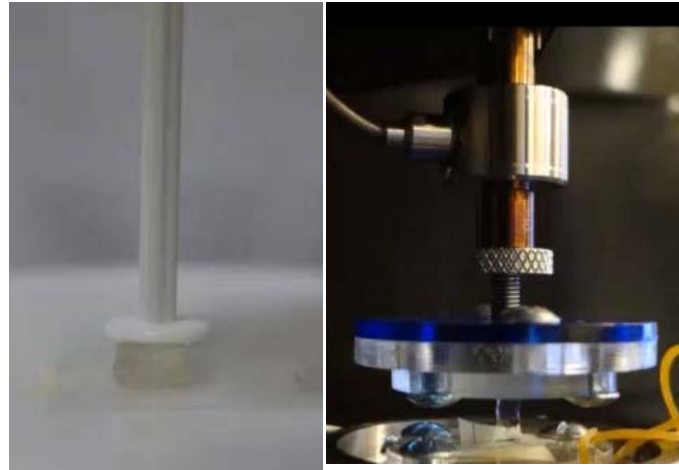
Feng Qian



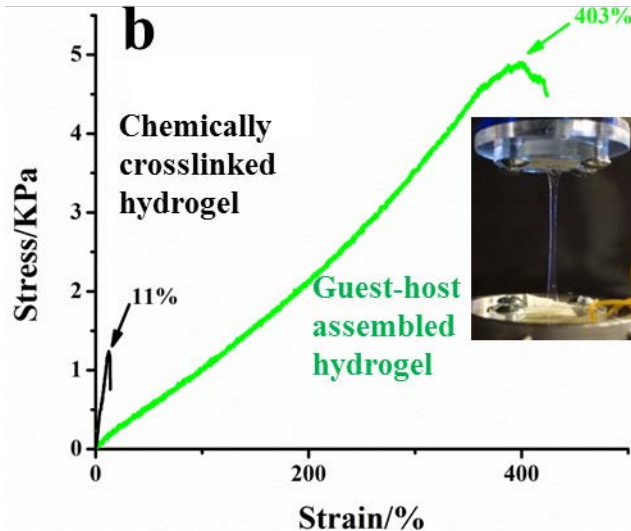
Dr. Wei Kongchang



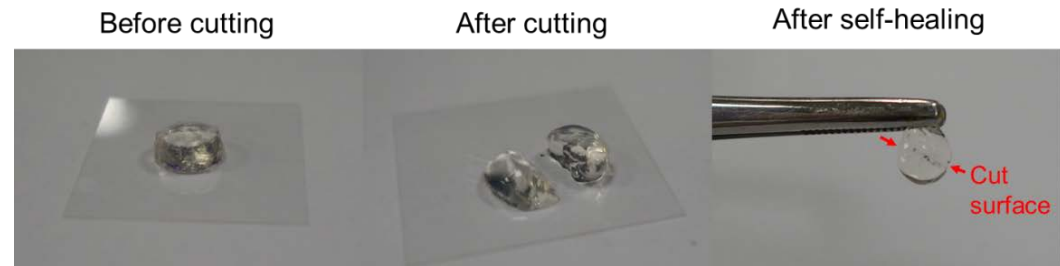
Regular gel with irreversible chemical crosslinking



Supramolecular gel with reversible crosslinking

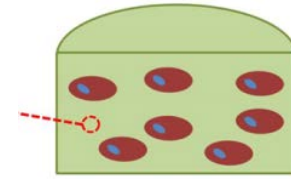
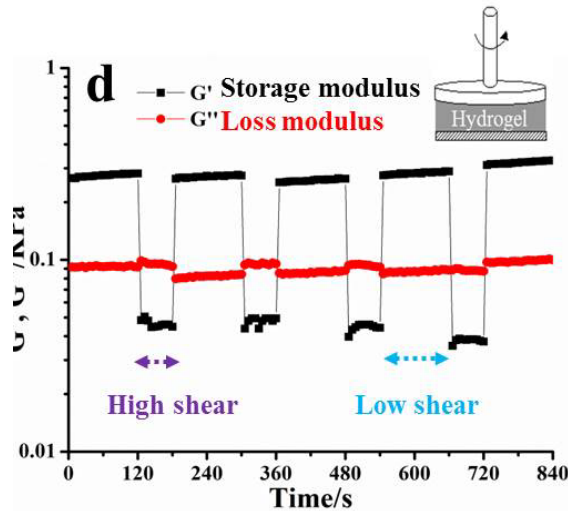


## Self-healing of the broken supramolecular hydrogel

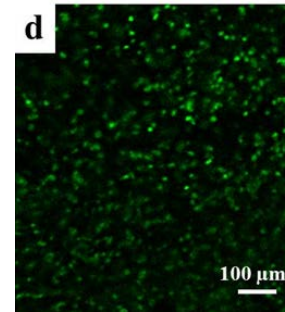


# Superior Injectability of the supramolecular hydrogels

## Shear-thinning property

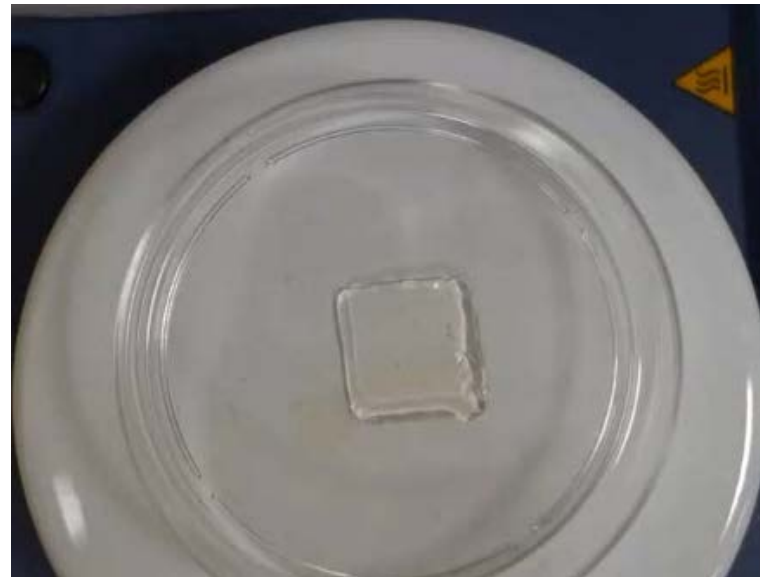


Cells encapsulated in 3D hydrogel



Stem cells in the hydrogel remain viable (green cells) after injection through a needle

- Injectable in the gelation state
- Hydrogel can be pre-loaded with cells or drugs before injection
- Easy handling by the surgeons in the operation theatre



Feng Qian



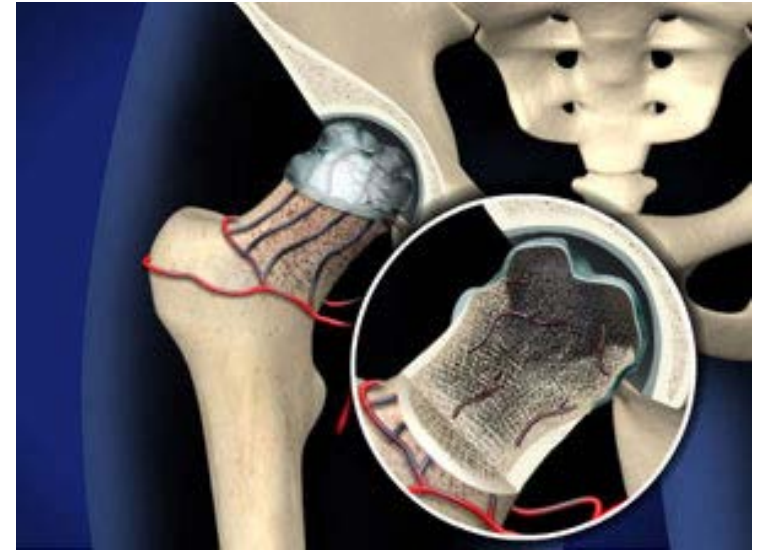
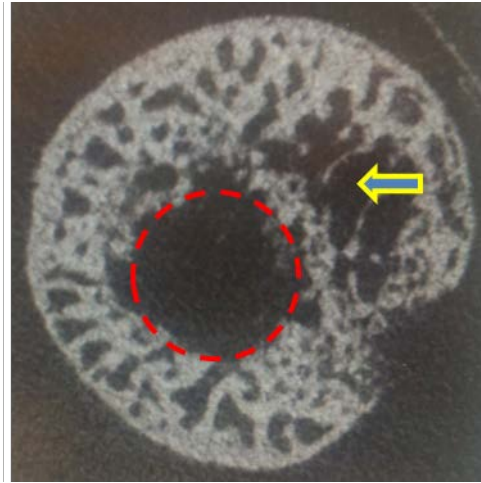
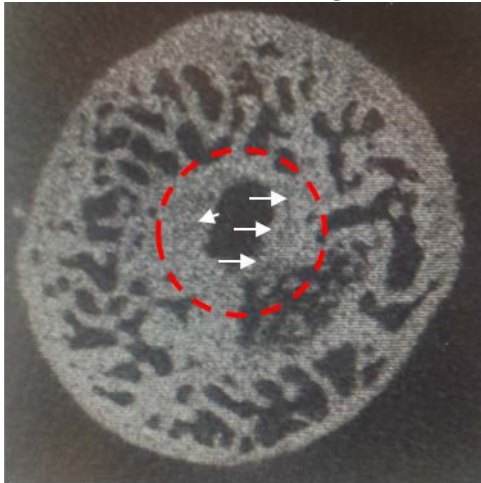
Dr. Wei Kongchang



# MSC-seeded supramolecular hydrogels for repairing necrotic femoral head

Hydrogel loaded with stem cell & drug

Control



**The red circles indicate the tunnel created for core decompression**

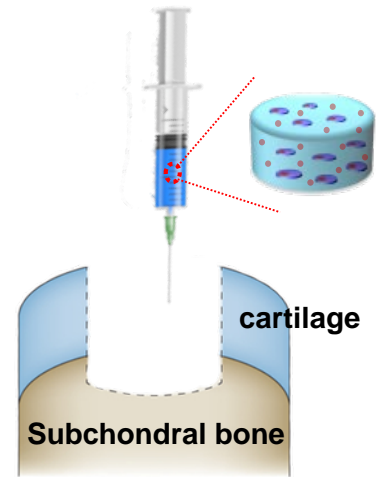
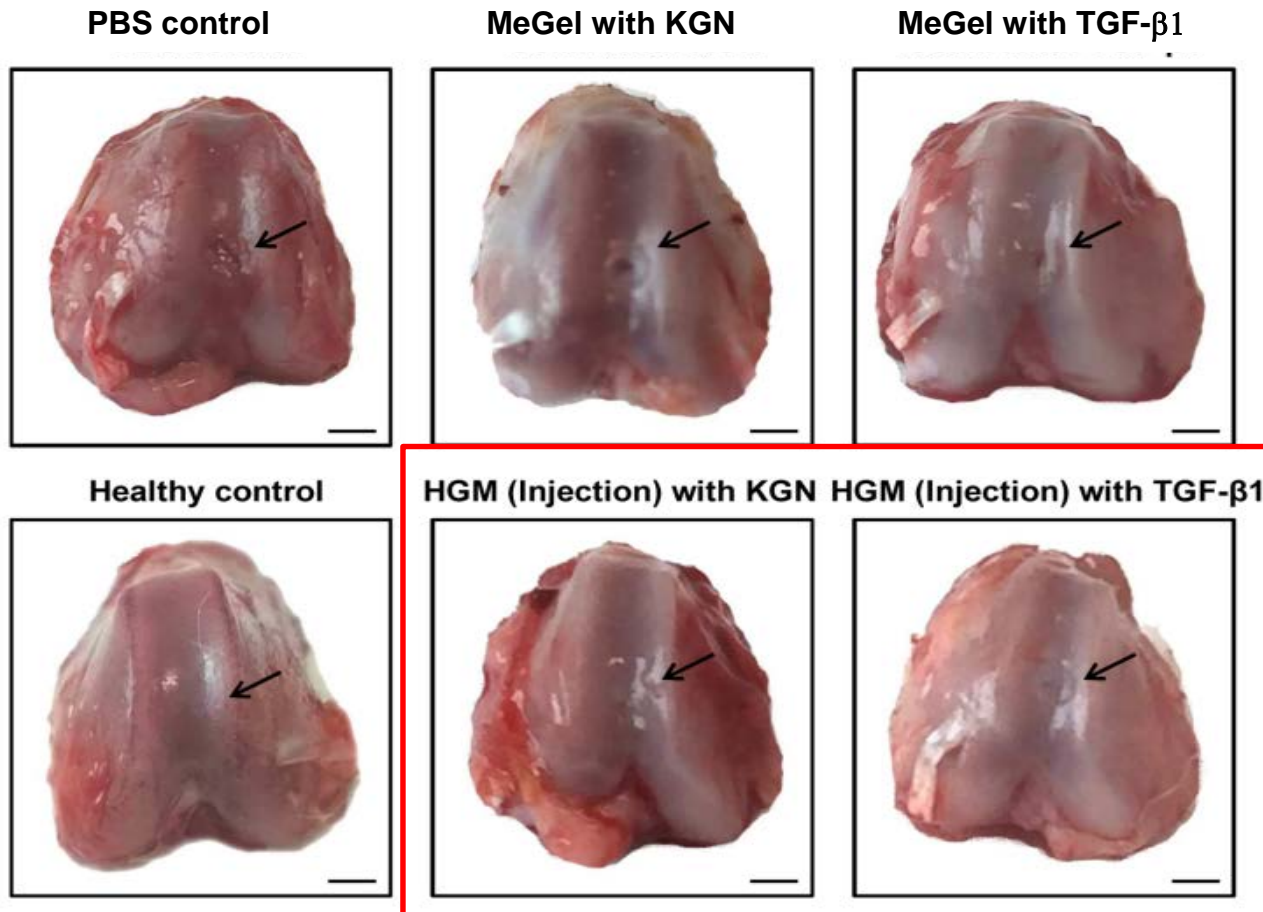
**White arrow: new bone formation within the tunnel**

**Yellow arrow: dead bone resorption**

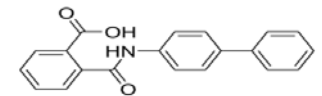


In collaboration with  
Prof. Qin Ling, Orthopedic &  
Traumatology, CUHK

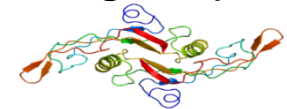
# HGM gelatin hydrogels encapsulated with MSCs and drugs promote osteochondral regeneration in vivo



Hydrogels are injected into the defects



**Kartogenin (KGN)**



**TGF- $\beta$ 1**



In collaboration with Prof. Li Gang, Orthopedic & Traumatology, CUHK

The cell and drug laden HGM hydrogels:

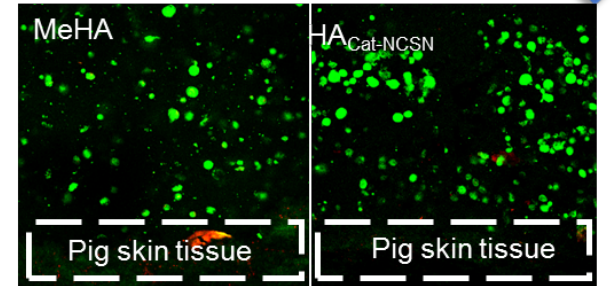
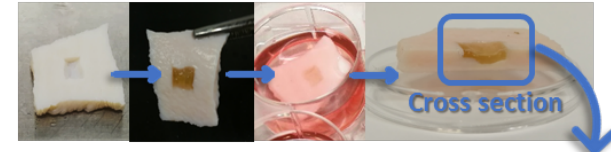
- injected into the osteochondral defects
- adhering to the defects
- Complete healing of the defects with regenerated tissue

Scale Bar: 2 mm.

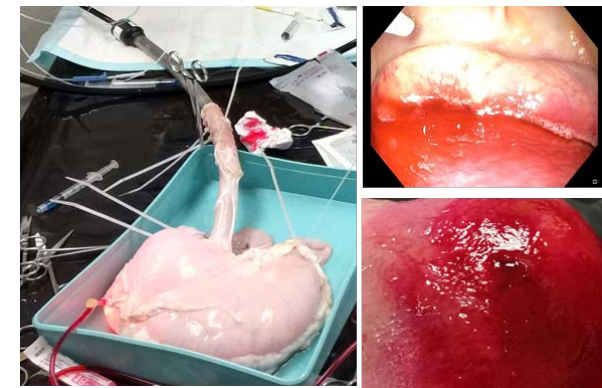
# A fast-gelation, bio-adhesive, and pH-independent hydrogels for treating gastric ulcers



Xiayi Xu



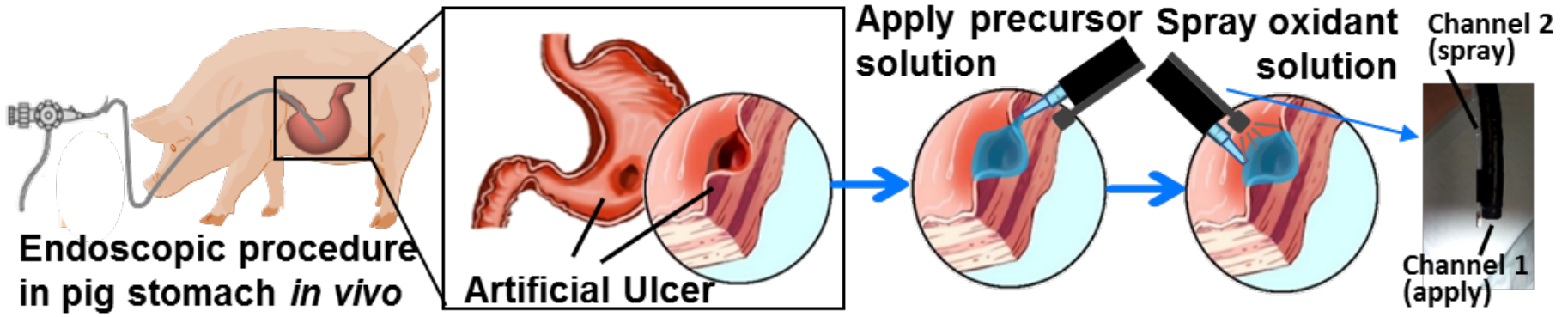
**Encapsulation of stem cells in these adhesive hydrogels**



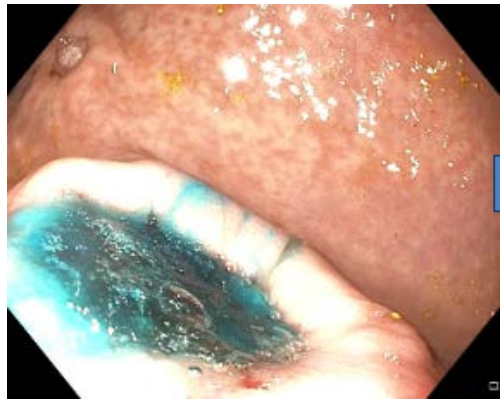
**Hemostatic hydrogels to arrest upper GI hemorrhage**

- **Ultra-fast gelation (< few seconds) and bioadhesive hydrogels under broad pH range (2-9)**
- **Potential application for cell/drug delivery to acidic gastric tissue to treat diseases such as peptic ulcer and GI hemorrhage**

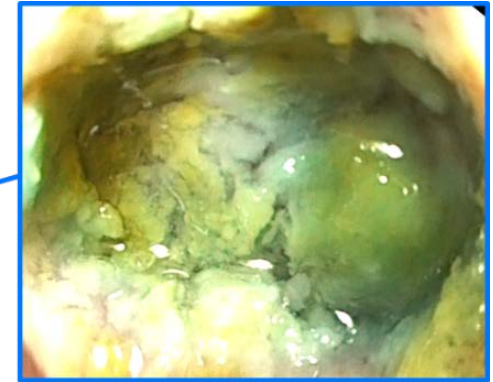
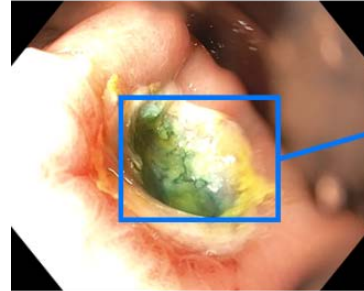
Unpublished



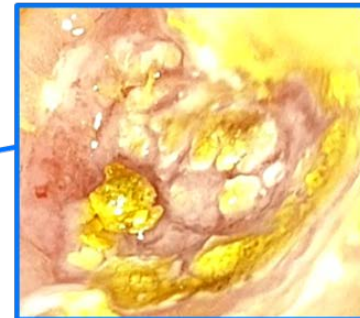
24 hour later



Adhesive Hydrogel



Empty Control

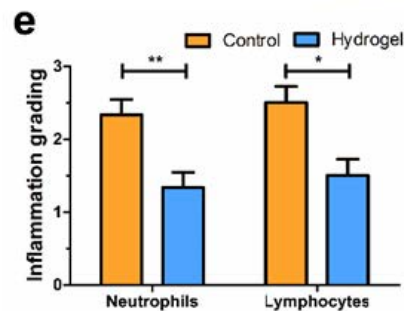
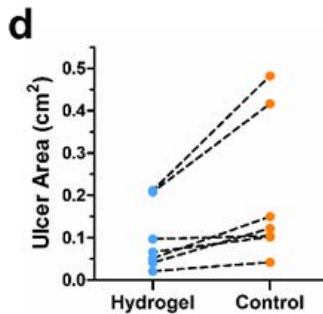
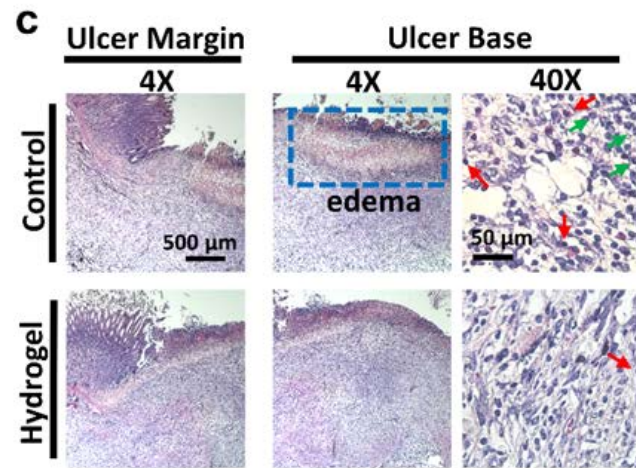
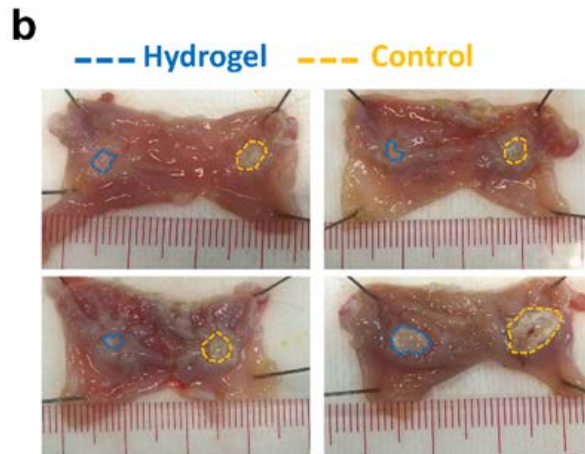
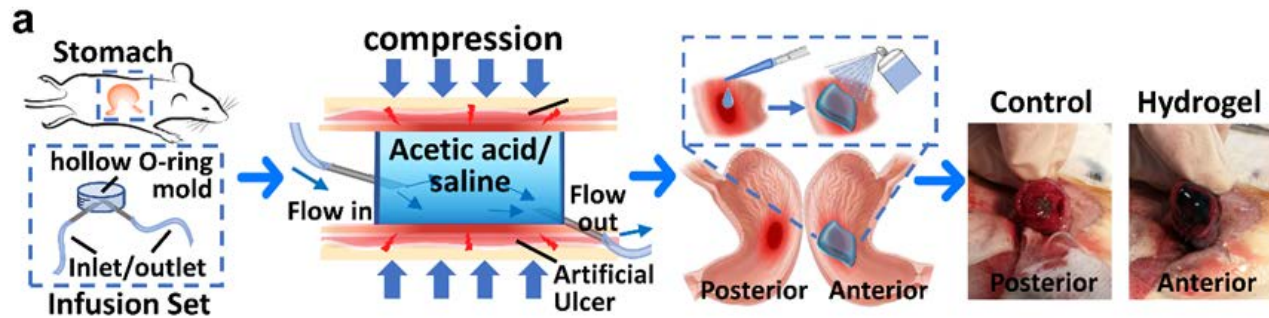


Hydrogels cover and adhere to the ulcer owing to ultra-fast gelation and bio-adhesion

Prof. Phillip Chiu



# Hydrogel treatment promoted healing of gastric ulcers

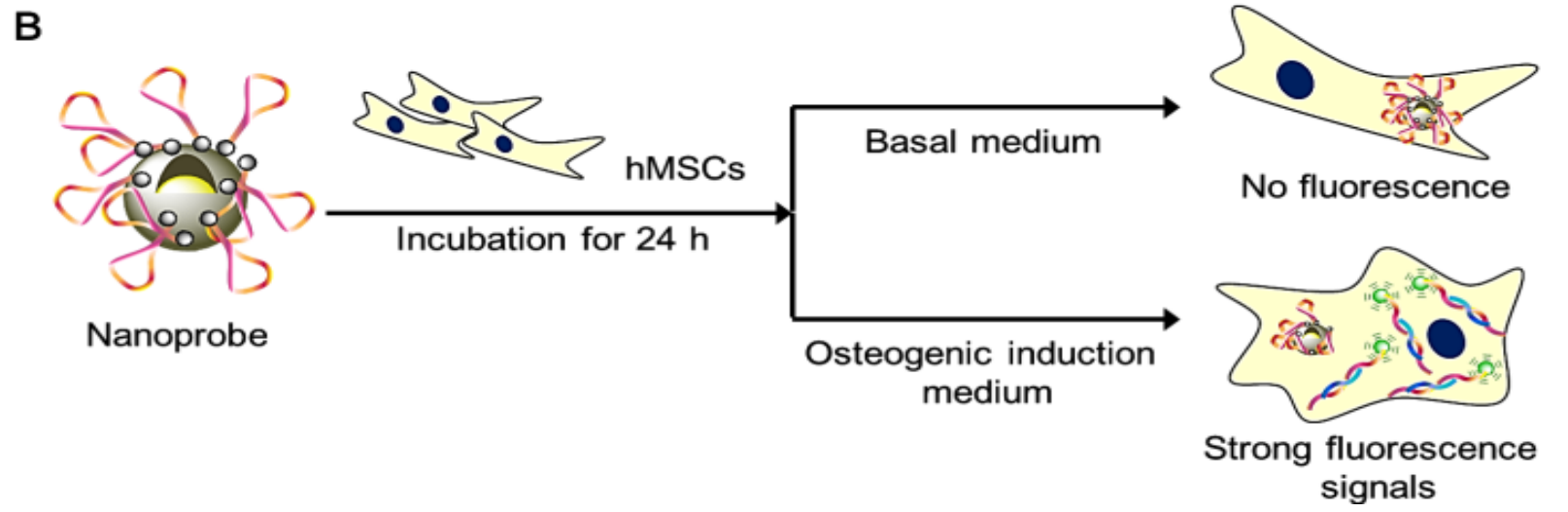
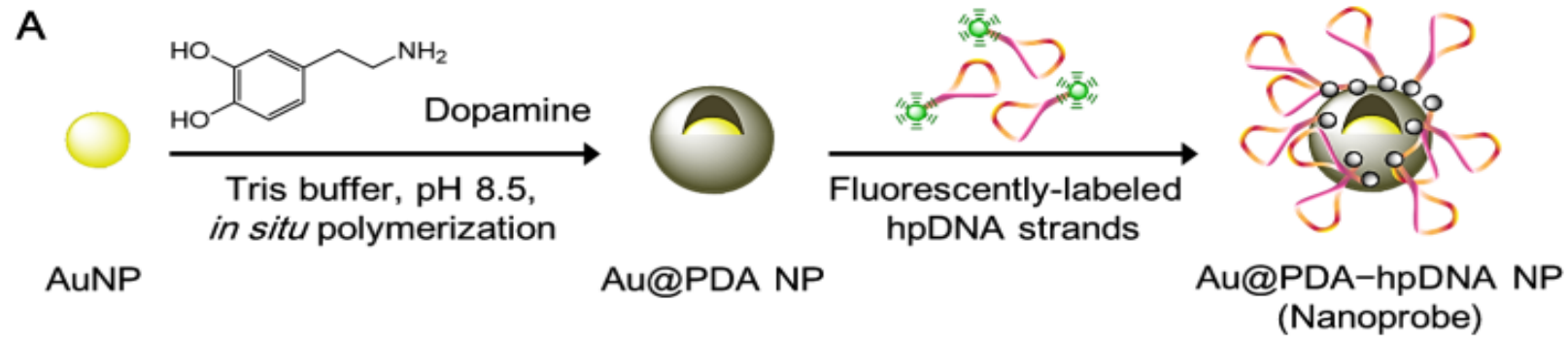


Xiayi Xu

# Au@PDA Nanoprobe to detect miRNA in living stem cells

## Gold@PDA-hpDNA nanoprobe

Choi Chun Kit

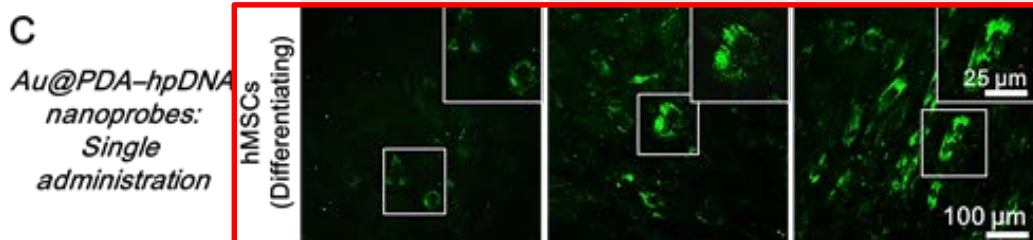
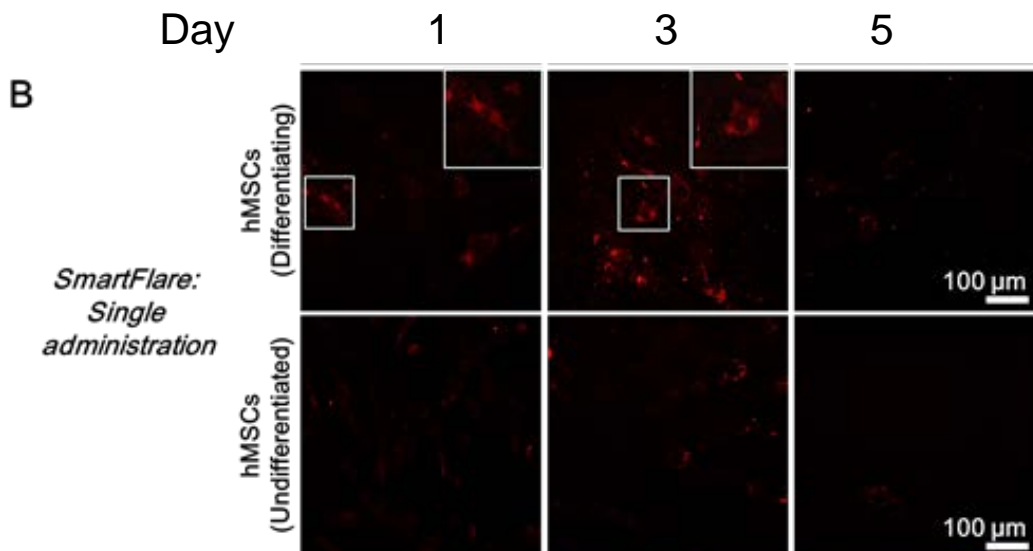






# Benchmark against SmartFlare™ (Merck Millipore)

## Comparison with SmartFlare™

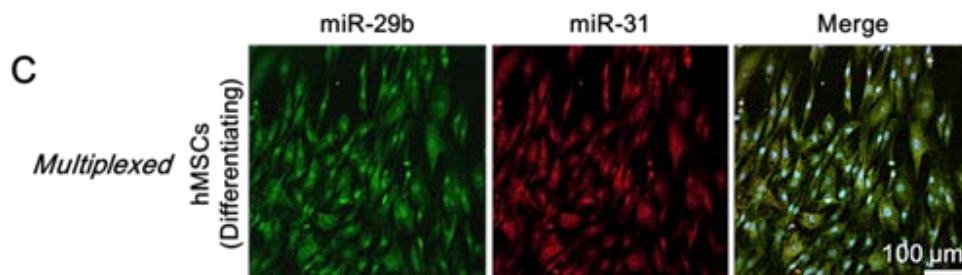


**Our gold@PDA nanoprobe enables long term monitoring of miRNA expression level in living stem cells.**

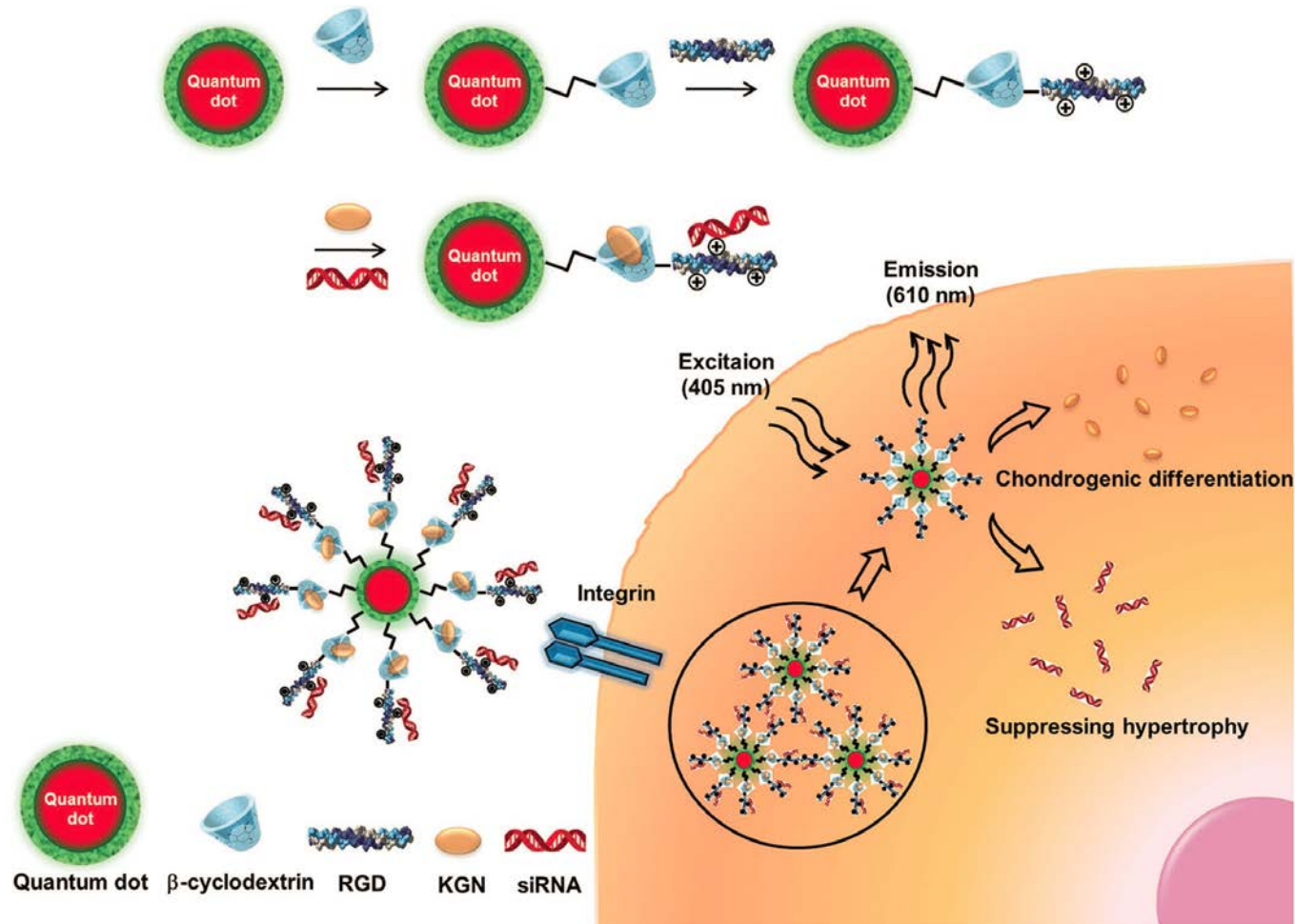
### Advantages:

- Live cell detection
- Long term tracking
- Robust signal
- Modular design
- No transfection agent
- Easy fabrication

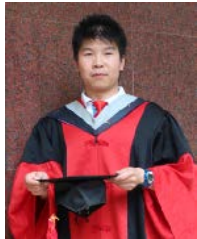
## Simultaneous detection of multiple miRNA targets



# Multifunctional nanocarrier for codelivery of the small molecules and siRNA to control stem cell differentiation



Dr. Xu Jianbin

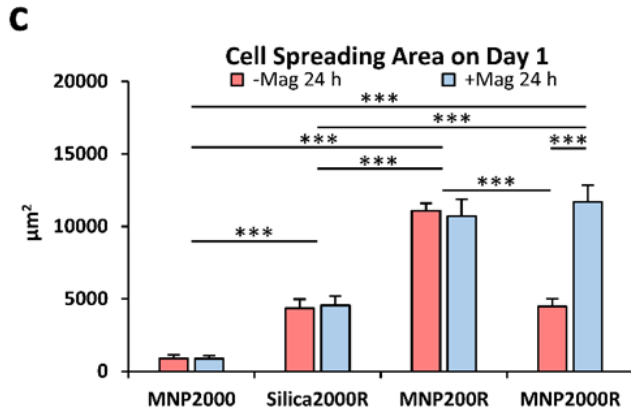
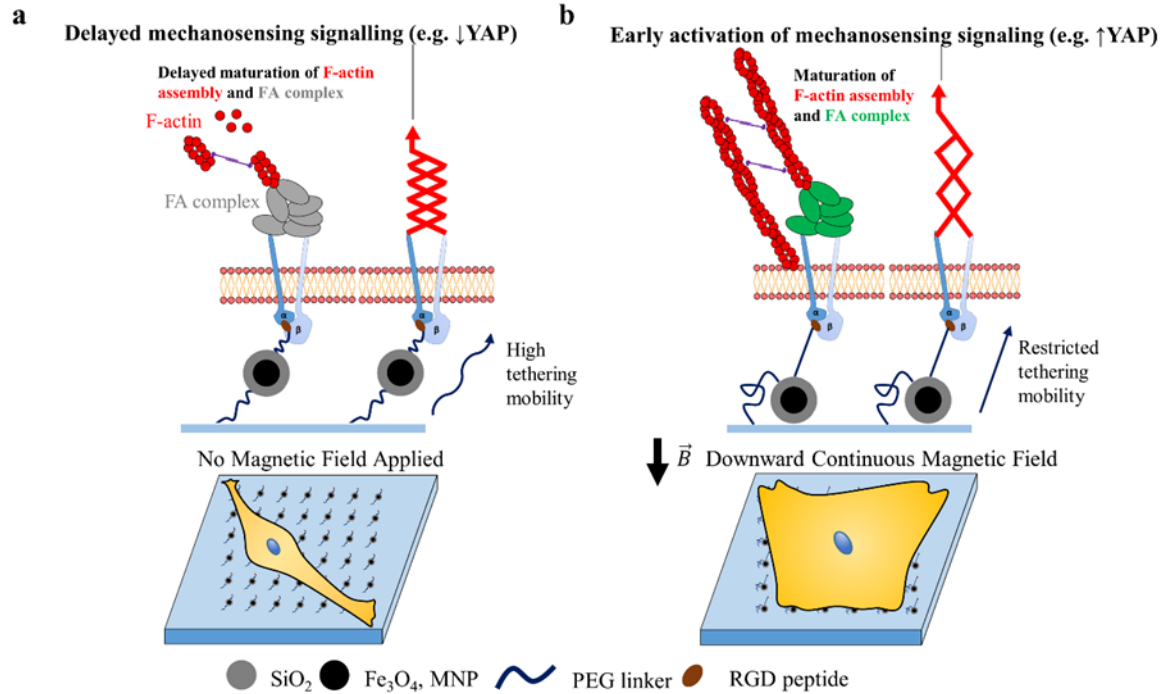
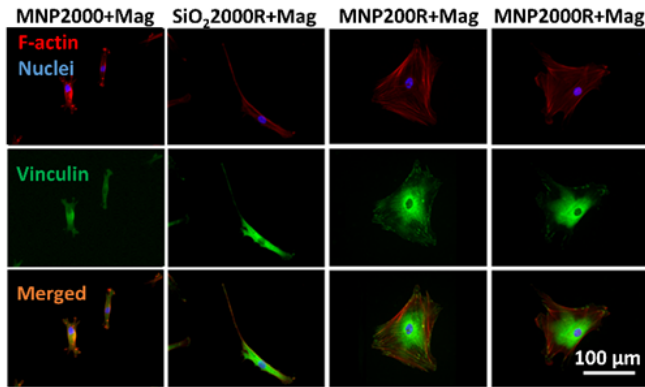


Dr. Li Jinming

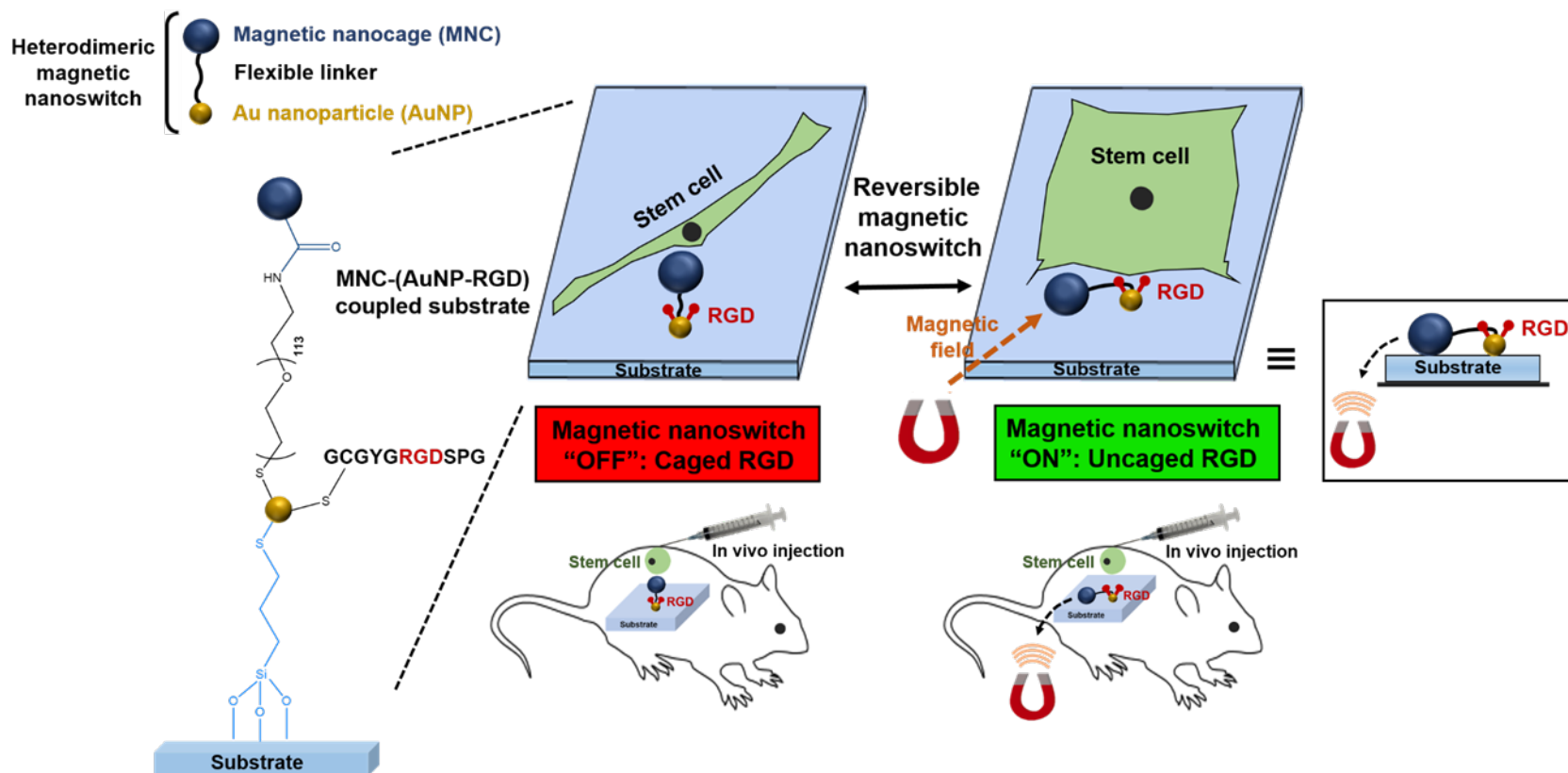


# Magnetically tuning the integrin ligand tether mobility regulate hMSCs adhesion and differentiation

Dexter Wong



# Reversible magnetic nanocaging of RGD-bearing AuNP-MNP heterodimer



**Under external magnetic field, magnetic nanoswitch reversibly uncaged and caged RGD**

# Selected journal publications from 2015.6 to present published by my students/postdocs

- +Kang, H.; et al.; \*Bian, L. Remote control of heterodimeric magnetic nanoswitch regulates the adhesion and differentiation of stem cells. *J. Am. Chem. Soc.*, 2018;140 (18): 5909-5913. (IF: 14.357)
- +Kang, H.; et al.; \*Bian, L. Magnetic manipulation of reversible nanocaging controls in vivo adhesion and polarization of macrophages. *ACS Nano*, accepted. (IF: 13.709)
- +Li, R.; et al.; \*Bian, L. Multiscale reconstruction of a synthetic biomimetic micro-niche for enhancing and monitoring the differentiation of stem cells. *Biomaterials*, 2018,173:87-99. (IF: 8.806)
- +Kang, H.; et al.; \*Bian, L. Remote manipulation of ligand nano-oscillations regulates adhesion and polarization of macrophages in vivo. *Nano Letters*, 2017, 17 (10), 6415-6427. (IF: 12.080)
- Wei, K.; et al.; \*Bian, L. Multivalent host-guest hydrogels as fatigue resistant 3D matrix for excessive mechanical stimulation of encapsulated cells. *Chem. Mater.* 2017, 29 (20), 8604-8610. (IF:9.890)
- Zhu, M.; et al.; \*Bian, L. Bio-adhesive polymersome for localized and sustained drug delivery at pathological sites with harsh enzymatic and fluidic environment via supramolecular host-guest complexation. *Small*, 2018 Feb;14(7). (IF: 9.598)
- +Kang, H.; +Wong, S.H.D.; Yan, X.; Jung, H.J.; King, S.K.; Lin, Si.; Wei, K.; Li, G.; \*David, V.; \*Bian, L. Remote control of multi-Modal nanoscale ligand oscillations regulates stem cell adhesion and differentiation". *ACS Nano*, 2017, 11 (10), 9636-9649. (IF: 13.709)
- +Li, R.; +et al.; \*Bian, L.; Self-assembled N-cadherin mimetic peptide hydrogels promote the chondrogenesis of mesenchymal stem cells through inhibition of canonical Wnt/ $\beta$ -catenin signaling. *Biomaterials*, 2017, 145: 33-43. (IF: 8.806)
- Zhang, K.; et al.; \*Bian, L. Self-assembled injectable nanocomposite hydrogels stabilized by bisphosphonate-magnesium (Mg<sup>2+</sup>) coordination regulates the differentiation of encapsulated stem cells via dual crosslinking. *Advanced Functional Materials*. 2017, 27, 1701642. (IF: 13.325)
- Li, J.; et al.; \*Tang, B.Z.; \*Bian, L. Photo-controlled siRNA delivery and biomarker-triggered AIEgen emission by upconversion NaYF<sub>4</sub>:Yb<sup>3+</sup>+Tm<sup>3+</sup>@SiO<sub>2</sub> nanoparticles for inducing and monitoring stem cell differentiation. *ACS Appl. Mater. Interfaces*, 2017 March. (IF: 8.097)

# Selected journal publications from 2015.6 to present published by my students/postdocs

- +Li, J.; et al.; \*Bian, L. Near-infrared light-triggered release of small molecules for controlled differentiation and long-term tracking of stem cells in vivo using upconversion nanoparticles. *Biomaterials*, 2016 Dec; 110: 1-10. (IF: 8.806)
- Dexter Wong, et. al., \*Bian, L. Magnetically Tuning Tether Mobility of Integrin Ligand Regulates Adhesion, Spreading, and Differentiation of Stem Cells. *Nano Letters*, 2017 (IF: 13.779)
- +Feng, Q.; +Wei, K.; Lin, S.; Xu, Z.; Sun, Y.; Shi, P.; Li, G.; \*Bian, L. Mechanically resilient, bioadhesive, and injectable supramolecular gelatin hydrogels crosslinked by weak host-guest interactions assist cell infiltration and in situ tissue regeneration. *Biomaterials*, 2016 Sept, 101: 217-28. (IF: 8.806)
- +Xu, J.; +Li, J.; Lin, S.; Wu, T.; Huang, H.; Zhang, K.; Su, Y.; Yeung, K.W.K.; Li, G.; \*Bian, L. Nanocarrier-mediated codelivery of small molecular drugs and siRNA to enhance chondrogenic differentiation and suppress hypertrophy of human mesenchymal stem cells. *Advanced Functional Materials*. 2016 Mar. DOI: 10.1002/adfm.201504070. (IF: 13.325)
- Wei, K.; Zhu, M.; Su, Y.; Xu, J.; Feng, Q.; Lin, S.; Wu, T.; Xu, J.; Tian, F.; Xia, J.; Li, G.; \*Bian, L. Robust biopolymeric supramolecular “Host-Guest Macromer” hydrogels reinforced by in situ formed multivalent nanoclusters for cartilage regeneration. *Macromolecules*, 2016 Jan, 49 (3), pp 866–875. (IF: 5.554)
- Zhu, M.; Lin, S.; Sun, Y.; Feng, Q.; Li, G.; \*Bian, L. Hydrogels functionalized with N-cadherin mimetic peptide enhance osteogenesis of hMSCs by emulating the osteogenic niche. *Biomaterials*, 2016 Jan, Vol.77: 44–52 (IF: 8.806)
- Choi, C.K.; Xu, Y.; Wang, B.; Zhu, M.; Zhang, L.; \*Bian, L. Substrate coupling strength of integrin-binding ligands modulates adhesion, spreading, and differentiation of Human mesenchymal stem cells. *Nano Letters*, 2015 Oct 14;15(10):6592-600. (IF: 12.080)
- Choi, C.K.; Li, J.; Wei, K.; Xu, Y.; Ho, L.W.; Zhu, M.; To, K.W.; \*Choi, C.H.; \*Bian, L. A gold@polydopamine core-shell nanoprobe for long-term intracellular detection of microRNAs in differentiating stem cells. *J. Am. Chem. Soc.*, 2015 Jun 17;137(23):7337-46. (IF: 14.357)

# Our patents

- US patent: osteochondral implants, arthroplasty methods, devices and systems. Inventors: Hung C.T, Ateshian, G.A, Lima, E.G., Cook, J.L., Bian, L. Publication number: US 2010/0036492 A1
- US patent (US 9,889,086 B2): A bioadhesive and injectable hydrogel. Inventors: Feng, Q.; Wei, K.; Lin, S.; Li, G.; Bian, L.
- US patent: Nano-constructs for polynucleotide delivery. Inventors: Choi, C.K.; Choi, C.H.; Bian, L.
- US/China patent: A fast, pH-independent, and efficient conjugation method. Inventors: Xu, Y.; Zhao, P.; Wei, K.; Bian, L.
- US/China patent: Scalable and versatile method for preparing single-chain nanoparticles. Inventors: Chen, X.; Wei, K.; Bian, L.
- US/China patent: Injectable hydrogels that promote mineralization and afford sustained release of bioactive ions. Inventors: Zhang, K.; Bian, L.
- US provisional patent: Rapid modification of polysaccharide-based material. Inventors: Chen, H.; Bian, L.
- US provisional patent: In situ synthesis of organic fluorophores in a polymeric matrix. Inventors: Chen, H.; Bian, L.

# Awards

Meiling winning the Fondazione Trainee Award in the World Biomaterial Congress hosted in Montreal, Canada (May, 2016)



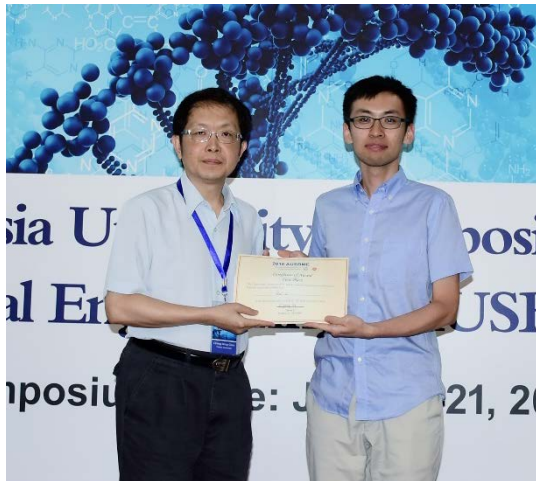
Feng Qian winning the Best Poster Award in the Nature Biomaterials and Tissue Engineering Conference (April, 2016)



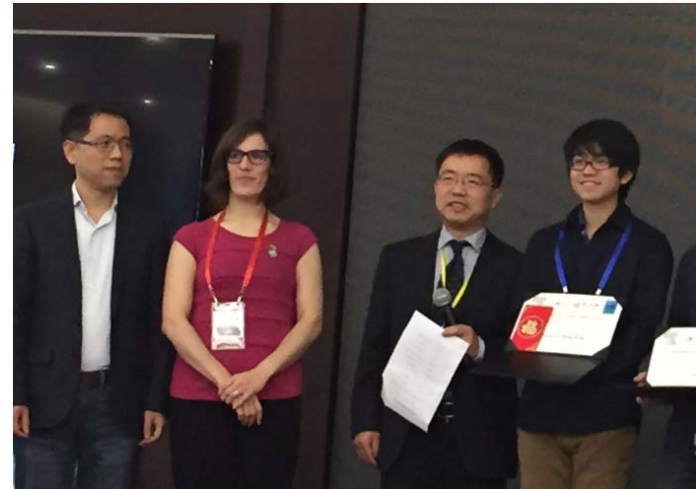


# Awards

Li Rui winning the Best Paper Award in AUSBME conference (July, 2016)

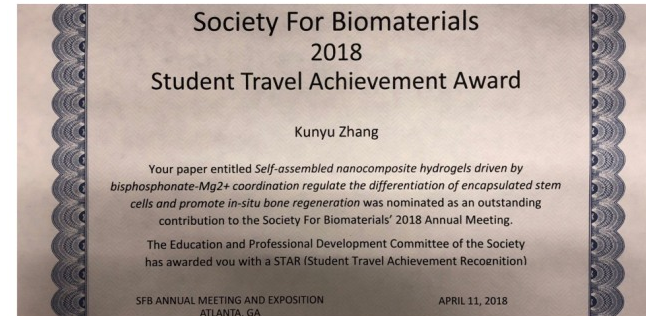


Dexter Wong winning the Best Paper Award in NanoMed conference (Jan, 2017)



# Awards

Meiling Zhu winning the CUHK FoE best PhD thesis award (2018)



Kunyu Zhang winning the Student Travel Achievement Award and Star Abstract Award from SFB annual meeting, Atlanta, USA, 2018.

# Collaboration

**Prince of Wales Hospital,  
Orthopaedics and Traumatology, CUHK**

Prof. Kai Ming Chan Prof. Qin Ling Prof. Li Gang



**Electrical  
engineering, CUHK**

Prof. Jonathan Choi



**Chemistry, CUHK**

Prof. Xia Jiang Prof. Ngai To Prof. Chan Hsiao Chang



**SBS, CUHK**

**Orthopaedics and  
Traumatology, HKU**

Prof. Yan Chun-Hoi Dr. Wen Chunyi



**Mechanical  
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Prof. Anderson  
Shum



**Chemistry,  
HKUST**

Prof. Tang  
Benzhong



**Electrical  
Engineering,  
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**Mechanical and  
Biomedical  
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Prof. Shi Peng



**Shenzhen 2<sup>nd</sup>  
People's hospital**

Prof. Wang  
Daping



## Biomaterials & Stem Cell Tissue Engineering Laboratory

<http://www.bme.cuhk.edu.hk/lbian/>

### Postdoc

- Dr. Wei Kongchang
- Dr. Heemin Kang
- Dr. Boguang Yang
- Dr. Yin Chao

### Ph.D. students

- Zhang Kunyu
- Li Rui
- Zhao Pengchao
- Chen Xiaoyu
- Dexter Wong
- Xu Xiayi
- Yuan Weihao

### RA

- Ricky Wong

### Funding

- Research Grant Council, Hong Kong
- Innovation Technology Commission, Hong Kong
- National Science Foundation of China
- Health Medical Research Fund, Hong Kong
- Shun Hing Institute of Advanced Engineering



*Thank you!*

## Biomaterials & Stem Cell Tissue Engineering Laboratory

Lab website

<http://www.bme.cuhk.edu.hk/lbian>



Lab website QR code

Students with **diverse background** in biology, chemistry, polymer, physics, material science, biomedical engineering, chemical engineering, etc. **are all welcome to apply!**

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