BIOGRAPHICAL SKETCH

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NAME: Tong, Xinming

eRA COMMONS USER NAME (credential, e.g., agency login): tong.xinming

POSITION TITLE: Instructor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Beijing Institute of Technology, Beijing, P.R. China	B.S.	06/2004	Polymer Science
Beijing Institute of Technology, Beijing, P.R. China	Ph.D.	06/2009	Material Science and Engineering
Tsinghua University, Beijing, P.R. China	Postdoctoral	06/2011	Polymer chemistry and Biomaterials
Stanford University, CA, USA	Postdoctoral	02/2016	Biomedical Engineering

A. Personal Statement

I am an experienced research scientist with training and expertise in the fields of polymer chemistry, material science and biomedical engineering. I am highly motivated to pursue an academic research career to contribute my expertise to the field of biomedical research by developing novel materials tools for biology and medicine. My Ph.D. research training focused on polymer chemistry, in which I developed novel methods that allow control of the sequence of and structure of cyclodextrin based polyrotaxanes. I have comprehensive experience in polymer design, synthesis and characterization. I also led a research grant as a PI sponsored by National Science Foundation of China (NSFC), in which I gained valuable experience in leading a project and team to deliver results within timeline and budget. After my Ph.D. study, I have expanded my research from basic polymer chemistry to designing biomaterials for medical applications such as vitreous substitute through a two-year postdoctoral research at Tsinghua University in China. Since 2011, I joined the Stem Cells and Biomaterials Engineering Laboratory at Stanford University under the guidance of Prof. Fan Yang, which enabled me to learn new research fields such as stem cell biology and tissue engineering. My research has been focusing on developing novel biomaterials as stem-cell niche for elucidating how complex niche cues regulate stem cell fate, as well as enhancing stem cell-based bone repair. I have published 33 papers, 17 conference presentations, and 4 issued patents. My work has been published in leading journals in the field of biomaterials research including *Advanced Materials, Biomaterials, Acta Biomaterialia* and *Tissue Engineering*. My papers have been cited over 400 times with a h-index of 12.

B. Positions and Honors

Positions and Employment

2004-2009 Graduate Student Fellow, Material Science, Beijing Institute of Technology, P.R. China.
2009-2011 Postdoctoral Fellow, Chemical Engineering, Tsinghua University, P.R. China.
2011-2016 Postdoctoral Fellow, Departments of Orthopaedic Surgery, Stanford University, CA, USA
2016-2018 Research Scientist, Department of Orthopaedic Surgery, Stanford University, CA, USA
2018-present Instructor, Department of Orthopaedic Surgery, Stanford University, CA, USA

Honors

2009 Outstanding Graduate Student, Beijing Institute of Technology

2011 National Postdoctoral Fellowship of China
2011 Young Scholar Grant from National Science Foundation of China

C. Contributions to Science (selected from a total of 30 publications)

1. **Development of novel injectable biomaterials as 3D stem cell niche to enhance differentiation and tissue formation in 3D.** Stem cells have been used as promising recourses in cell based therapies and tissue regeneration. Efforts have been dedicated to identifying optimal soluble factors and insoluble niche properties to regulate stem-cell differentiation. While extensive studies have been done under this paradigm, most of them are performed in 2D culture. However, the efficiency of stem-cell differentiation and tissue formation in 3D is often substantially lower due to the physical constraint. It remains challenge to achieve efficient stem-cell differentiation and tissue formation for successfully tissue regeneration. I have been dedicating efforts to deal with the limitations in two ways. *First, we have developed* 3D *macroporous* scaffolds crosslinked from microribbon-like hydrogels in the presence of cells. The scaffolds allow independently tuning of biochemical, mechanical, and topographical properties. We have shown that the macroporosity substantially enhanced the cell survival, proliferation, differentiation and matrix deposition. *Secondly, we developed a sliding hydrogel with mobile crosslinks and biochemical ligands* that is suitable for use as a 3D stem-cell niche. We have demonstrated that the molecular mobility of the sliding hydrogel allows stem cells to reorganize the surrounding ligands and change their morphology in 3D, supporting more efficient stem-cell differentiation toward multiple lineages. The sliding hydrogel constitutes a versatile material for supporting differentiating stem cells toward desired lineages in 3D, which is essential for stem-cell based tissue regeneration.

   a. Tong, X.; Yang, F., Sliding hydrogels with mobile molecular ligands and crosslinks as 3D stem cell niche. Adv. Mater., 2016, 28 (33), 7257-63.
   b. Han, L.H.; Tong, X.; Yang, F., Photocrosslinkable PEG-based microribbons for forming 3D macroporous scaffolds with decoupled niche properties, Adv. Mater. 2014, 26, 1757-62.
   c. Han, L.; Yang, F.; Tong, X. "Macroporous 3-D scaffolds for tissue engineering". (US Patent 9402710 B2, 2016.)
   d. Yang, F.; Han, L.; Tong X. "Dynamic macropore formation using multiple porogens". (US Patent 9415138 B2, 2016.)

2. **Development of hydrogel platforms with independently tunable biochemical and mechanical properties to decipher cell-niche interactions.** How cell behaviors are regulated by microenvironmental cues attracted extensive efforts and investigations. To facilitate understanding cell-niche interactions, hydrogels have been widely used as artificial cell niche given their tissue-like water content as well as tunable chemical and physical properties. However, few hydrogels developed to-date allow independent tuning of niche properties such as biochemical signals and mechanical stiffness. To overcome the limitations, I have successfully developed hydrogels as platform materials with independently tuned biochemical ligand incorporation, mechanical stiffness and degradation. With the platform materials, our findings demonstrated that behaviors and phenotype of cells are influenced synergistically by various niche signals. These platform materials will also help further elucidate stem-cell interactions and identify optimal scaffold compositions for promoting desirable cellular processes and tissue formation.

   a. Tong, X.; Yang, F., Interpenetrating network hydrogel as biomimetic cell niche with independently tunable biochemical and mechanical properties, Biomaterials 2014, 35, 1807-1815.
   b. Wang, C.; Tong, X.; Yang, F., Bioengineered 3D brain tumor model to elucidate the effects of matrix stiffness on glioblastoma cell behavior using PEG-based hydrogels, Mol. Pharm. 2014, 11, 2115-2125.
   c. Tong, X.; Jiang, J.; Zhu, D.; Yang, F., hydrogels with dual gradients of mechanical and biochemical cues for deciphering cell-niche interactions, ACS Biomater. Sci. Eng., 2016, 2, 845-852.

3. **Development and evaluation of a polymer hydrogel as long-term stable vitreous substitute.** Vitrectomy to treat vitreoretinal diseases needs to remove the primary vitreous body, and a substitute is required after surgery to support the retina or block the retinal break. However, none of the vitreous substitutes in current clinical can be used for long-term application due to their short retention time and various complications. To solve this limitation, my efforts dedicated to the development and evaluation of

an in situ crosslinked and hydrolysis-resistant hydrogel as a long-term vitreous substitute material. The hydrogels we developed showed good biocompatibility and were tolerated well in the rabbit vitreous cavity at a follow-up of as long as 9 months. Our studies also lead to 2 patents.

a. Tao, Y.; Tong, X.; Zhang, Y.; Lai, J.; Huang, Y.; Jiang, Y.-R.; Guo, B.-H., Evaluation of an in situ chemically crosslinked hydrogel as a long-term vitreous substitute material. Acta Biomater. 2013, 9, 5022-30.
b. Tong, X.; Lai, J.; Guo, B.; Huang, Y., A new end group structure of PEG for hydrolysis-resistant biomaterials. J. Polym. Sci., Part A: Polym. Chem. 2011, 49, 1513-1516.
c. Tao, Y.; Jiang, Y.; Guo, B.; Huang, Y.; Tong, X. "Application of in-situ crosslinking hydrogel capable of intraocular injection in preparing artificial vitreous bodies". (Chinese Patent CN 101934089, 2013.)
d. Tong, X.; Guo, B.; Lai, J.; Huang, Y., "Polymers that react with thiol groups and form hydrolysis-resistant linkages". ('Chinese Patent CN 101885841, 2012.)

4. **Development of a strategy to synthesize vinyl copolymers with accurate control on the sequence of the monomer units.** In polymer chemistry, sequence-controlled polymer synthesis is one of the ultimate goals of scientists. Even the greatest progress of controlled polymerization chemistry in the past decades can only control the sequence of blocks of monomers, but not the precise sequence at the monomer level, not to mention a general strategy for synthesis. To address this, we used a single-monomer addition by atom-transfer radical polymerization to allow monomer-level sequence control in synthesizing vinyl copolymers. We have successfully proved the feasibility of strategy we proposed and provided a method to achieve sequence control of vinyl copolymers.

   a. Tong, X.; Guo, B.; Huang, Y., Toward the synthesis of sequence-controlled vinyl copolymers. Chem. Comm. 2011, 47, 1455-1457.

5. **Optmized synthesis of cyclodextrin based polyrotaxanes (PRs).** Cyclodextrin (CD) based polyrotaxane is featured by the structure with ring shaped cyclodextrin molecules threaded on the linear polymer axle chains locked by the end-capping reagent. It has attracted broad interests since its invention, due to the fancy structure and various potential applications. However, the synthesis of PR was usually tedious, under poor control and with low yield. My early research efforts have dedicated to improving the efficiency of the synthesis and controlling the structure, which includes the end-capping method, the coverage and the threading sequence of the CD rings on the axle polymer chains. We have successfully developed facile methods to synthesis PRs with increased the yields. In addition, using polymer segment as end-capping reagents led to advanced properties of the resulting PR, which include improved the solubility in various solvents, self-assemble into nanoparticles and ease of fabrication into scaffolds. I served as primary investigator in some of the studies.

   a. Yan, X.; Yang X.; Tong X.*; Huang Y.*, A method to accelerate the gelation of disulfide-crosslinked hydrogels, Chinese J. Poly. Sci. 2015, 33, 118-127. (*Corresponding author)
   b. Song, Q., Luo, Z.; Tong, X.*; Du, Y.; Huang, Y., Glutathione as the end capper for cryclodextrin/PEG polyrotaxanes, Chinese J. Poly. Sci. 2014, 32, 1003-1009. (*Corresponding author)
   c. Tong, X.; Gao, P.; Zhang, X.; Ye, L.; Zhang, A.; Feng, Z., End-capping double-chain stranded polypseudorotaxanes using lengthily tunable poly(2-hydroxyethyl methacrylate) blocks via atom transfer radical polymerization. Polym. Int. 2010, 59, 917-922.
   d. Tong, X.; Zhang, X.; Ye, L.; Zhang, A.; Feng, Z., Synthesis and characterization of block copolymers comprising a polyrotaxane middle block flanked by two brush-like PCL blocks. Soft Matter 2009, 5, 1848-1855.
   e. Tong, X.; Zhang, X.; Ye, L.; Zhang, A.; Feng, Z., Novel main-chain polyrotaxanes synthesized via ATRP of HEMA initiated with polypseudorotaxanes comprising BriB-PEG-iBBr and alpha-CDs. Polymer 2008, 49, 4489-4493.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/10gzdgU-kSVQI/bibliograpahy/47871837/public/?sort=date&direction=descending

D. Additional Information: Research Support and/or Scholastic Performance

Completed Research Support

Young Scholar Grant from NSFC *21004038* *01/2011 – 01/2013*
A method for synthesizing co-polyrotaxane with controlled number and sequence of threaded cyclodextrin
The goal of this project is to develop a method to synthesize cyclodextrin (CD) based polyrotaxane with controllable CD threading, in the aim of exploring and studying the potentially therapeutic application of such "mobile" multivalent ligand.
Role: PI