COLLOQUIUM (2015-12)

School of Materials Science & Engineering

"Heparin conjugates for medical applications"

Prof. Byun, Youngro

(Dept. of Molecular Medicine and Biopharmaceutical Sciences, Seoul National University)

2015. 12. 03. (Thur.) 16:00

APRI 1F, Auditorium Hall

HEPARIN CONJUGATES FOR MEDICAL APPILCATIONS

Youngro Byun, Ph.D.

Department of Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology, and College of Pharmacy, Seoul National University

Polysaccharide is one of compounds that compose our body and it is involved in many different physiological reactions. Among them, heparin, mucopolysaccharide located on cell membrane and ECM, is widely used as anticoagulant drug. In our study, we are preparing the library of heparin conjugates for the medical applications.

Firstly, we developed orally active heparin by tconjugating with tetraDOCA (deoxycholic acid). The conjugated *tetra*DOCA interacted with several hydrophobic grooves in the substrate-binding pocket of ASBT. Orally absorbed LHe-*tetra*D successfully prevented thrombosis in a rat model of deep vein thrombosis. We believe that the 'receptor-like' functional transformation of ASBT can motivate the development of practical systems by synthesizing specific, high-affinity binding substrates, which enable transporter-based uptake of macromolecules. Thus, the functional transformation process of ASBT could lead to overcoming the size limitation in ASBT-mediated drug transport and can propose the new pathway for the oral macromolecular drug delivery.

Secondly, LMWH-Taurocholate conjugate (LHT7) was developed as tumoeal angiogenesis inhibitor. Vascular endothelial growth factor 165 ($VEGF_{165}$) dependent Matrigel plug assay and bFGF dependent HUVECs tubular formation test were performed to verify the antiangiogenic potential of LHT7 as an $VEGF_{165}$ and bFGF inhibitor. Finally tumor growth inhibition effects of LHT7 were investigated in SCC7 and MDA-MB231 xenograft mouse models. Apart from other heparin derivatives, LHT7 which has 12.7% of anticoagulant activity showed peculiar polyproline–helical structure. The results of HUVECs tubular formation and Matrigel plug assay bolstered the action of LHT7 as an antiangiogenic agent inhibiting $VEGF_{165}$ as well as bFGF functions. In tumor growth inhibition experiments, LHT7 showed a significant tumor growth inhibition potential on SCC7; moreover it delayed a development of MDA-MB231 effectively. Polyproline-helical structured LHT7 showed significant antiangiogenic potential and tumor growth inhibitory effect.

Short BIOGRAPHY: Youngro Byun

EDUCATION

1984 Feb	Seoul National University
	Department of Chemical Engineering (B.S.)
1986 Feb	Korea Advanced Institute of Science and Technology (KAIST)
	Department of Chemical Engineering (M.S.)
1994 Aug	The University of Utah
	Department of Pharmaceutics and Pharmaceutical Chemistry (Ph.D.)

WORK EXPERIENCES

1986 Mar – 1989 Nov	Researcher
	Division of Polymer Chemistry
	Korea Institute of Science and Technology (KIST)
1994 Aug – 1996 Aug	Post-Doc fellow
	Department of Pharmaceutics
	The University of Michigan
1996 Sep –2005 Aug	Associate/Assistant Professor
	Department of Materials Science and Engineering
	Gwangju Institute of Science and Technology (GIST)
2005 Sep – present	Professor/Associate Professor
	College of Pharmacy
	Seoul National University
2009 Sep – present	Professor
	WCU Department of Molecular Medicine and Biopharmaceutical Science,
	Graduate School of Convergence Science and Technology
	Seoul National University

RESEATCH AREA

- Therapeutic Glycobiologics
- Oral Drug Delivery System
- Induced Phenotype Targeting Metronomic Maintenance Chemotherapy
- Genetically Engineered Cell Therapy

RESEARCH ACTIVITIES

Associated Editor: Biomaterials (IF 8.557): 2014 ~ present

Editorial Board Member: Scientific Reports (IF 5.578): 2015 ~ present

Editorial Board Member: Pharm Res (IF 3.420): 2006 ~ present

> 140 SCI papers, > 40 patents