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Molecular structure of membrane proteins in Neurodegenerative disease

Identifying the tertiary structure of cellular membrane proteins at the atomic level is essential to fundamentally understand the principles of life phenomena. Transmembrane signaling receptors account for about 5% of the total human genome and mediate complex communication processes between cells and outside environment. Signaling receptors studies are critical to the development of the pharmaceutical industry as well as the basic science because they are targeted by almost all protein therapeutics. Previously, I have been studying the crystal structure of proteins related to immune diseases. Since joining here, we have been interested in membrane proteins structure related to degenerative brain diseases including Alzheimer's disease, neuroinflammation of neuron-microglia communication, and synapse proteins (such as receptors, adhesion molecules, signaling scaffolds, signaling molecules, and cytoskeletal proteins) known to constitute excitatory synapses, which work together to mediate neurotransmission and regulate synaptic plasticity.

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|---------------|---|------------------------------|--|
| Aim | Molecular structure of target protein and development of drug candidate | | |
| Tool | Structure biology+X-ray crystallography+cryo-EM+Antibody engineering | | |
| TARGET | <p>GPCR, SLC family</p> | <p>X-ray, cryo-EM</p> | <p>Lead screening (Fragment Based Drug Discovery)</p> <p>Structure based antibody optimization</p> |

Key techniques • Membrane protein biochemistry, X-ray crystallography, cryo-EM, Protein engineering

Research keywords • Membrane protein, Structure biology, Small molecule screening, Antibody optimization

Research Interests/Topics

1. Molecular structure of membrane protein using X-ray crystallography and cryo-EM
2. Structure-based drug candidate (lead screening, antibody optimization) discovery
3. Synapse protein interactome, Synaptopathy (Synaptic protein-related brain dysfunction)

Curriculum Vitae

2016~Present : Principal Investigator, KBRI
 2015~2016 : Postdoctoral Fellow, Dept. of Pharmacy,
 Korea Univ., Korea
 2005~2014 : Postdoctoral Fellow, Researcher, Protein
 Structure Research Team, KBSI, Korea
 2002~2004 : Researcher, CrystalGenomics Inc. and Dept.
 of Chemistry (Membrane Receptor Research
 Center), KAIST, Korea
 2001~2002 : Researcher, BioKorea Inc., Korea

Academic Credential

2012 : Ph.D., Pharmacy, Chungbuk Nat'l University
 2001 : M.S., Biochemistry, Chungnam Nat'l University
 1999 : B.S., Biochemistry, Chungnam Nat'l University

Awards/Honors/Memberships

2018~present : Women's Bioscience Forum (WBF) operation committee member
 2016~present : Member, Korean Society for Brain and Neural Sciences
 2002~present : Member, Korean Society for Structural Biology
 2001~present : Member, Korean Society for Molecular and Cellular Biology

Research Publications (selected)

- Park BB, Choi JW, Park D, Choi D, Paek J, **Kim HJ**, Son SY, Mushtaq AU, Shin H, Kim SH, Zhou Y, Lim T, Park JY, Baek JY, Kim K, Kwon H, Son SH, Chung KY, Jeong HJ, Kim HM, Jung YW, Lee K, Lee KY, Byun Y, Jeon YH. Structure-Activity Relationships of Baicalein and its Analogs as Novel TSLP Inhibitors. *Scientific reports*, 19;9(1):8762, 2019.
- Lee JJ*, **Kim HJ***, Yang CS*, Kyeong HH, Choi JM, Hwang DE, Yuk JM, Park K, Kim YJ, Lee SG, Kim D, Jo EK, Cheong HK, Kim HS. A high-affinity protein binder that blocks the IL-6/STAT3 signaling pathway effectively suppresses non-small cell lung cancer. *Molecular Therapy*, 22(7):1254-1265, 2014. (*co-first)
- Lee Y, Lee JJ, Kim S, Lee SC, Han J, Heu W, Park K, **Kim HJ**, Cheong HK, Kim D, Kim HS, Lee KW. Dissecting the critical factors for thermodynamic stability of modular proteins using molecular modeling approach. *PLoS One*, 21;9(5):e98243, 2014.
- Yeo KJ, Kim EH, Hwang E, Han YH, Eo Y, **Kim HJ**, Kwon O, Hong YS, Cheong C, Cheong HK. pH-dependent structural change of the extracellular sensor domain of the Drak histidine kinase from *Streptomyces coelicolor*. *Biochem Biophys Res Commun.*, 15;431(3):554-9, 2013.
- Han J*, **Kim HJ***, Lee SC, Hong S, Park K, Jeon YH, Kim D, Cheong HK, Kim HS. Structure-based rational design of a Toll-like receptor 4 (TLR4) decoy receptor with high binding affinity for a target protein. *PLoS One*, 7(2):e30929, 2012. (*co-first)
- Lee SC*, Park K*, Han J*, Lee JJ*, **Kim HJ** Hong S, Heu W, Kim YJ, Ha JS, Lee SG, Cheong HK, Jeon YH, Kim D, Kim HS. Design of a binding scaffold based on variable lymphocyte receptors of jawless vertebrates by module engineering. *Proc Natl Acad Sci USA*, 109(9):3299-304, 2012. (*co-first)

Patents (selected)

- KR: Method for effective purification of human TREM2 proteins using recombinant baculovirus. (Appl. No. 10-2018-0122539, 2018-10-15)
- KR: Monoclonal antibody with specificity for human TREM2 protein, hybridoma cell line producing the same and use thereof. (Appl. No. 10-2018-0129740, 2018-10-29)
- US: Method for improving repebody containing repeat modules. (Appl. No. 14/538778(PF-B1404-US), 2014-11-13)
- US: Repebody for novel interleukin-6 and use thereof. (Appl. No. 14/381407(PF-B1401-US), 2014-08-27)
- KR: Method for improving repebody containing repeat module. (Appl. No. 10-2013-0137700, 2013-11-13)
- WO, KR: Repebody for novel internalin-6 and use thereof. (Appl. No. PCT/KR2013/001605, 2013-02-27, Appl. No. WO2013129852A1, 2013-09-06)
- KR: Novel polypeptides binding with interleukin-6 and uses thereof. (Appl. No. 10-2013-0007380, 2013-01-23)
- KR: Crystallization method for recombinant variable lymphocyte receptors of jawless vertebrates. (Appl. No. 10-2011-0141410, 2011-12-23)