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Aquaporin 5 (AQP5) activates the epidermal growth factor receptor (EGFR) and Src, potentially through its novel kinase activity, and may be involved in Iressa resistance

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The role of aquaporin water channels in human carcinogenesis (AQPs) recently has become an area of great interest. We have previously demonstrated that AQP5 can promote cell proliferation leading to tumorigenesis by activation ERK1/2 pathways and that the expression of AQP5 is associated with prognosis of lung cancer, colon cancer and CML. Here, we provide evidences that these phenomenon may be mediated by activation of EGFR and/or Src, upstream signal for ERK1/2. Cellular hyperplasia and activation of ERK1/2 in transgenic mice carrying human AQP5 over-expression construct confirms our prior findings *in vivo*. Expression of AQP5 activate EGFR and Src in BEAS cells and HCT116 cells by increasing phosphorylation of both EGFR and Src, and inhibition of AQP5 expression lead to decreased phosphorylation of both molecules with decreased ERK1/2 activation. The association of AQP5 with EGFR and Src are demonstrated by immnoprecipitation and immnofloursecnce examinations in BEAS cells and such interaction is inhibited by mutation in PKA site in AQP5. Furthermore, by using baculovirus system, recombinant hAQP5 (rAQP5) was purified, which shows a unique kinase activity *in vitro* and that rAQP5 can synergistically increase overall kinase activity when combined with EGFR and Src. Based on these findings, we demonstrate that AQP5 may be involved in the development of Iressa (a small molecular inhibitor for EGFR) resistances, possibly through modulating phosphorylation of EGFR. While these observations provide several novel findings, studies for the detailed mechanistics leading to activation of EGFR and Src by AQP5 are warranted in the future.

Biography

Dr. Chulso Moon MD, PhD is a board certified medical oncologist in US and has been working in Johns Hopkins University (JHU) since 2001 as tenure track faculty, attending physician in the department of otolaryngology/oncology and JHU Cancer Center. Presently, he is actively participating in the cancer research as adjunct professorship in JHU and also mentoring graduate student in human genetics program in Johns Hopkins Medical School. He is an MD, PhD physician scientist participating both academic research and patient care. He obtained his PhD in human genetics from JHU under Dr. Peter Agre (2003 Novel Laureate) and finished his medicine and oncology training in MD Anderson Cancer Center. He played a key role in characterizing the role of AQPs in human cancer by providing the first model of AQP5 as a novel therapeutic target. Additionally, he has published several key review articles in clinical oncology focused on head and neck and prostate cancer.