C-reactive Protein contributes to Breast Cancer Progression via Integrin α2 and Fcγ receptor

Aree Moon, Eun-Sook Kim, Sun Young Kim, Minsoo Koh, Joohee Jung, PhD, Duksung Women's University, South Korea
Hye-Min Lee, Kyoungmee Kim, MS, Duksung Women's University, South Korea
Hoe Suk Kim, Woo Kyung Moon, PhD, Seoul National University Hospital, South Korea
Sejin Hwang, MD, Hanyang University, South Korea

C-reactive protein (CRP) is an acute phase protein synthesized upon the inflammatory responses, associated with breast cancer. The process of tumor cell invasion and metastasis involves the adherence of cells to the extracellular matrix via integrin as a receptor for matrix molecules. The present study investigated the role of CRP in the adhesive phenotype of breast cells and the underlying mechanisms. Here, we first showed that CRP induces adhesion of MCF10A human breast epithelial cells through the activation of integrin α2 signaling. Expression of integrin α2 was induced by CRP in which transcription factors c-fos and SP1 may be involved. Binding of CRP with integrin α2 leads to the activation of focal adhesion kinase (FAK), paxillin and ERKs. CRP also binds to an Fcγ receptor I (FcγRI), and induces activation of paxillin, FAK and ERKs. Integrin α2 and FAK have crucial roles in the adhesive and invasive phenotypes as well as MMP-9 upregulation induced by CRP in MCF10A cells. Treatment with an inflammatory lipid sphingosine-1-phosphate induced CRP, which may be secreted and exert an autocrine effect by binding to FcγRI and integrin α2. Involvement of CRP in adhesion, invasion, anchorage-independent growth and upregulation of integrin α2, paxillin and FAK was observed in MDA-MB-231 triple-negative human breast cancer (TNBC) cells. Using an *in vivo* invasion model and an orthotopic mouse tumor model with MDA-MB-231 cells, we showed that CRP has an important role in intravasation and tumor growth *in vivo*, demonstrating the *in vivo* relevance of our *in vitro* results. The present study elucidates a critical molecular basis between CRP, integrin α2 and FcγRI pathways in MCF10A breast cells and MDA-MB-231 TNBC cells, thereby providing useful information on CRP-induced aggressiveness of breast cells in the inflammatory microenvironment.

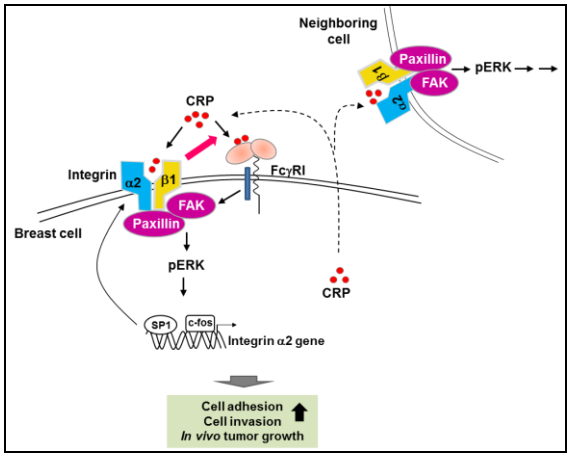

Fig. 1. A proposed model for the signaling networks for the CRP-induced activation of integrin α2 and FcγRI signaling leading to breast cell adhesion, invasion and *in vivo* tumor growth.

Biography

Aree Moon is a professor at College of Pharmacy, Duksung Women's University. She received her B.S. degree at College of Pharmacy, Seoul National University, Seoul, Korea in 1983. She moved to the USA and continued to study in Biochemistry. She got her Ph.D. degree at Department of Biochemistry and Biophysics, Iowa State University, Iowa, USA in 1989. Since 1995, she has been a professor at College of Pharmacy, Duksung Women's University. She has received a number of awards including 'the Presidential Award', 'the Order of Science and Technology Merit', and the 'Korea L'Oreal-UNESCO Award for Woman in Science'.

E-mail: armoon@duksung.ac.kr