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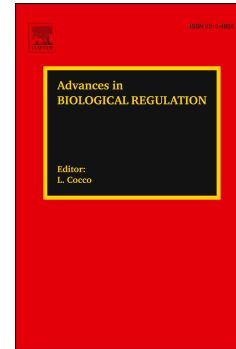
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## Sphingosine 1-phosphate and Cancer

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Key words: Sphingosine 1-phosphate, sphingosine kinase, sphingosine 1-phosphate receptors, cancer cell-fibroblast interactions, metastasis.

*Abstract*--The bioactive lipid, sphingosine 1-phosphate (S1P) is produced by phosphorylation of sphingosine and this is catalysed by two sphingosine kinase isoforms (SK1 and SK2). Here we discuss structural functional aspects of SK1 (which is a dimeric quaternary enzyme) that relate to coordinated coupling of membrane association with phosphorylation of Ser225 in the 'so-called' R-loop, catalytic activity and protein-protein interactions (e.g. TRAF2, PP2A and G<sub>q</sub>). S1P formed by SK1 at the plasma-membrane is released from cells via S1P transporters to act on S1P receptors to promote tumorigenesis. We discuss here an additional novel mechanism that can operate between cancer cells and fibroblasts and which involves the release of the S1P receptor, S1P<sub>2</sub> in exosomes from breast cancer cells that regulates ERK-1/2 signalling in fibroblasts. This novel mechanism of signalling might provide an explanation for the role of S1P<sub>2</sub> in promoting metastasis of cancer cells and which is dependent on the micro-environmental niche.

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