Baicalein inhibits epithelial–mesenchymal transition in human breast cancer cells by downregulating Cyr61 and LOXL-2

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Epithelial–mesenchymal transition (EMT), a critical step in the acquisition of a metastatic state, is an attractive target for therapeutic interventions directed against tumor metastasis. Cysteine-rich protein-61 (CCN1/Cyr61) has been implicated as an important mediator in the proliferation and metastasis of breast cancer. Hence, targeting Cyr61 and associated pathways may inhibit breast cancer cell growth and invasion. In the present study, we showed that baicalein inhibited significantly the expression of Cyr61 and migration and invasion of MDA-MB231 human breast cancer cells. Exposure to baicalein led to increased E-cadherin expression, possibly due to the ubiquitination of Snail and Slug, which is mediated by Akt down-regulation and glycogen synthase kinase 3β (GSK3β) activation. Furthermore, baicalein inhibited the expression of lysyl oxidase like-2 (LOXL-2) and subsequently attenuated the direct interaction between LOXL-2 and Snail or Slug, thereby enhancing GSK3β-dependent Snail and Slug degradation. Our findings provide new insights into the anti-metastatic mechanism of baicalein and may contribute to its beneficial use in breast cancer therapies.

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