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THERAPEUTIC TARGETING OF TFF3 INHIBITS ONCOGENESIS IN COLORECTAL CANCER

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Trefoil Factor 3 (TFF3) expression was observed to be upregulated in colorectal cancer (CRC) and correlated with distant metastasis and poor survival outcomes. The present study investigates the functional role of TFF3 and explores the potential of therapeutic inhibition of TFF3 in CRC alone and in combination with conventional chemotherapy. We demonstrated that the forced expression of TFF3 increased cell viability of CRC cells, being attributed to increased cell cycle S-phase entry and decreased apoptosis. Furthermore, the forced expression of TFF3 enhanced the capacity for foci formation and promoted the cancer stem cell-like behaviour of CRC cells. In contrast, the siRNA-mediated depletion of TFF3 decreased the oncogenicity of CRC cells as indicated by the above parameters. Furthermore, AMPC, a novel and selective small molecule inhibitor of TFF3, has been developed in our laboratory and is used to examine the functional implications of TFF3 inhibition in CRC cells. Consistently, AMPC inhibition of TFF3 in CRC cells resulted in reduction of oncogenic properties. Mechanistically, we demonstrate that the TFF3-stimulated oncogenic behavior of CRC cells is dependent on TFF3 activation of the MAPK/ERK pathway. Besides showing efficacy as a single agent, AMPC when used in combination with 5-fluorouracil (5-FU) exhibited a synergistic inhibitory effect, consistent with our observation that TFF3 depletion increased 5-FU sensitivity in CRC cells. In summary, our study highlights the potential of TFF3 as a therapeutic target in CRC and underscores the potential benefits of its pharmacological inhibition in this cancer using AMPC.

BIOGRAPHY

Rumei Chen received her BSc with academic excellence scholarship from Nan Kai University, China. Upon graduation, she was conferred a full-time PhD research scholarship offered by the Yong Loo Lin School of Medicine in National University of Singapore, Singapore. Her research focus revolves around the profiling of an estrogen-regulated oncogene (TFF3) in CRC and the development of novel therapeutic strategies against it. Meanwhile she has been accredited by Experimental Therapeutics Centre & D3 in Singapore during a course that educates scientists about conducting translational R&D theory and practice. From which, she learnt many practical guidance to translate basic research findings into full-fledged R&D projects. Other than research, she has been active in promoting science-related events such as assisting to organize the International Union of Basic and Clinical Pharmacology world conference. She is a member of many international committees, such as European Association for Cancer Research, Pharmacological Society of Singapore.

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