Using eicosapentaenoic acid to improve Cetuximab sensitivity in KRAS mutants

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Our previous studies showed that there may be better sensitivity to anti-EGFR antibody therapy in KRAS or BRAF mutants with increasing expression levels of miR-378. As known, miR-378 is embedded within PPARC1β, which encodes PGC-1β, and could be stimulated by feeding lauric acid in cells. Consequently, we tried to replace it with eicosapentaenoic acid (EPA), an omega-3 unsaturated fatty acid that is FDA-approved (Fig 1.). The western blotting and ELISA assay were performed to analyze the MAPK/ERK pathway and caspase pathway in three cell lines (SW480 and HCT116 with contain KRAS mutants, and HT29 with contain BRAF mutants), including cell lines before and after feeding with 40 μM concentration of EPA. All experiments were then compared to the wild type cells (caco2), the control cell line (Fig 2.).

**Results**

The results showed increased expression of miR-378 in all types of mutated cells, except the wild type CRC cells. The data demonstrated with EPA may indeed significantly induce the expression of miR-378, and further restore the sensitivity of anti-EGFR antibody in KRAS mutant cells.

**Conclusions**

KRAS mutant cells may restore sensitivity to Cetuximab after up-regulation of the miR-378 induced by EPA. This finding has offered a new alternative therapeutic solution for future patients suffering from KRAS mutated colorectal cancer.

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**Figure 1.** The hypothetical mechanism of stimulating the gene PGC-1β expression by EPA may potentially enhance the expression of miR-378.

**Figure 2.** Experiment flow chart.

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1. EPA
2. Cetuximab
3. EPA + Cetuximab

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