ATP Synthase: A Molecular Drug Target for Dietary Polyphenols

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Background: A variety of dietary polyphenolic compounds are known to bind and inhibit ATP synthase. Polyphenol led inhibitory studies on bovine mitochondrial and Escherichia coli ATP synthase suggest that the beneficial effects of dietary polyphenols are in part linked to the blocking of ATP synthesis in tumor cells, thereby leading to apoptosis. Our lab has studied the inhibitory effects of a variety of naturally occurring and structurally modified polyphenols/bioflavonoids on E. coli ATP synthase.

Method: Growth properties of wild type E. coli pBWU13.4 were tested on fermentable and non-fermentable carbon source before harvesting to isolate ATP synthase. Polyphenol induced inhibitory studies were performed on purified F1, membrane bound F1F0, wild type E. coli (positive control), and puC118 (negative control). Structural modification of polyphenols was done by repositioning or introduction of new functional groups.

Results: A large variation on the extent and potency of inhibition was observed for naturally occurring polyphenols. We found that structural modification can enhance the potency of less potent inhibitors on molar scale with no residual activity. These studies also resulted in the identification of differential inhibitory patterns of inhibition of ATP synthase. Our results have demonstrated that polyphenol modulation can enhance the inhibitory effects of some polyphenols by 100-fold. This study also shows that ATP synthase can be used as a potent molecular drug target for antimicrobial and antitumor polyphenols. Currently we are studying the synergetic effects of several biochemically modulated polyphenols on ATP synthase as well as on E. coli cells.

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