



A NEW ROLE FOR AN OLD HORMONE: GASTRIN – IRON INTERACTIONS

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Gastrins have been implicated as growth factors for colorectal cancer. We have discovered that gastrins bind ferric ions tightly and that, for some forms of the hormone, iron binding is essential for biological activity. We now plan to use chelating agents to remove the ferric ions and hence block the ability of gastrins to stimulate the growth of colorectal cancers. The animal models will include colorectal cancer cell lines grown as xenografts in nude mice and genetically modified mice more susceptible to developing colorectal cancer.

We will also investigate the role of gastrin in iron homeostasis. We have already shown that circulating gastrin concentrations are increased in mouse models of the iron overload disorder hemochromatosis. We now plan to extend these studies by measurement of gastrin concentrations in mice deficient in the iron regulatory molecules hepcidin and hemojuvelin and in humans with iron regulatory disorders.

Techniques:

- Animal models of disease
- Transgenic mice
- Cancer patient samples
- Western blots
- Cell transfection
- RT-PCR
- Radioimmunoassays and ELISA

Publications:

Pannequin J, Kovac S, Tantiongco JP, Norton RS, Shulkes A, Barnham KJ, Baldwin GS. A novel effect of bismuth ions: Selective inhibition of the biological activity of glycine-extended gastrin. *J Biol Chem* 2004; 279:2453-2460.

He H, Shehan BP, Barnham KJ, Norton RS, Shulkes A, Baldwin GS. Biological activity and ferric ion binding of fragments of glycine-extended gastrin. *Biochemistry*. 2004; 43:11853-61.

Smith KA, Kovac S, Anderson GJ, Shulkes A, Baldwin GS. Circulating gastrin is increased in hemochromatosis. *FEBS Letters* 2006; 580:6195-6198.