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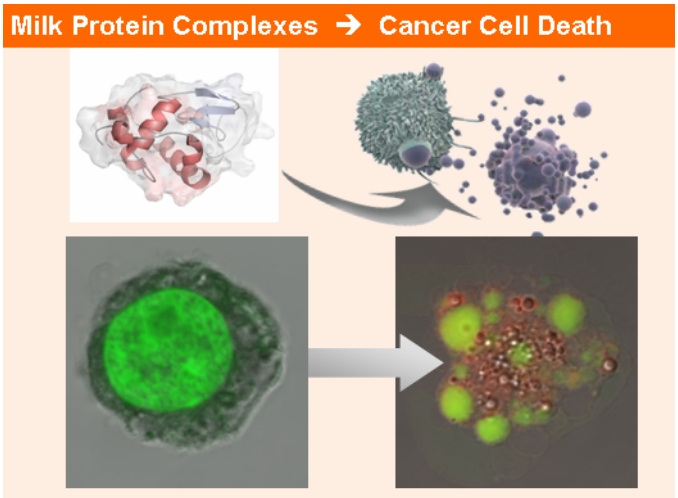
Biologically active complexes of bovine milk proteins



Key external stakeholders:

Scientific community, biotechnology start-up companies, Irish dairy companies, infant formula manufacturers

Practical implications for stakeholders:

- Processing of the whey protein α-lactalbumin does not impair its potential anti-tumour properties
- Some protein/fatty acid complexes may have the potential to be used for pharmaceutical purpose.

Main results:

Globular proteins such as α-lactalbumin and β-lactoglobulin can act as vehicles for delivering oleic acid to tumour cells, thereby inducing cell death by apoptosis.

Opportunity / Benefit:

The expertise and techniques developed for screening proteins as molecular delivery systems of bioactive components is available for interested companies and academic institutes.

Collaborating Institutions:

UCC and TCD

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Teagasc project team: Dr André Brodkorb (PI), Kamila Lišková (WF)
External collaborators: Prof Alan Kelly(UCC), Prof Nora O'Brien (UCC) and Prof Ken H. Mok (TCD)

1. Project background:

The whey protein α-lactalbumin (α-la) and the fatty acid oleic acid (OA), have recently been shown to form a complex under specific chromatographic conditions, called HAMLET/BAMLET*, which cause cell death by apoptosis to a variety of known tumour cells, while sparing healthy cells. α-lactalbumin is a major component in dairy ingredients

*HAMLET/BAMLET- Human/Bovine α-lactalbumin made lethal to tumour cells

2. Questions addressed by the project:

- What is the relationship between structural and biological properties of α-lactalbumin complexes with fatty acids?
- Are there implications for manufacturers of dairy ingredients that contain α-lactalbumin?

3. The experimental studies:

Chromatographic methods and cell culture techniques for purification, conversion and testing of α-lactalbumin and BAMLET were set up. Structural features of prepared complexes were studied by methods such as spectro-photometry, polyacrylamide gel electrophoresis, High Performance Liquid Chromatography (GP-, RP-HPLC), intrinsic tryptophan fluorescence, particle size, Fourier Transform Infrared spectroscopy (FTIR) and Nuclear Magnetic Resonance (NMR). Novel methods for conversion of α-lactalbumin into BAMLET were developed. The chemical structure of the complexes was correlated with the cytotoxicity towards tumour cells.

4. Main results:

The results of the project suggest that globular proteins such as α-lactalbumin and β-lactoglobulin can act as delivery vehicles for oleic acid to tumour cells, thereby inducing cell death by apoptosis. The cytotoxicity of the complex appears to be strongly dependent on the amount of bound oleic acid. The outcome of this project opens up a new field of research for the potential use of globular proteins as delivery vehicles of bioactive components.

Both α-lactalbumin and β-lactoglobulin may have a role to play in the prevention or limitation of tumours. However, more research is needed to identify their biological role *in vivo* during lactation or gastro-intestinal digestion.

Other results:

- It was shown that the cytotoxicity of BAMLET is independent of prior heat-induced denaturation or aggregation of α-lactalbumin.
- An analogous, BAMLET-like complex was prepared, by using a novel method, from β-lactoglobulin and oleic acid. The complex showed cytotoxicity towards U937 cells comparable with that of BAMLET. The mechanism of cell death was confirmed to apoptosis, as in the case of BAMLET.

5. Opportunity/Benefit:

The project has generated a number of methods for studying protein/fatty acid complexes and their bioactivity towards cancer cells. These expertises can be used by interested companies. A patent application has been filed by Teagasc covering process conditions for generating biologically active protein complexes.

6. Dissemination:

The research project resulted in 2 peer-reviewed publications, 1 patent and several oral presentations at international conferences (2 invited, 1 keynote lecture).

Note: due to the restrictions of the patent application, two further publication are awaiting submission for publication.

Main publications:

Brodkorb *et al.* (2010). A process for producing a biologically active globular protein complex. Patent Application number WO2010131237 (A1).

Lišková *et al.* (2011) *Cytotoxic complexes of sodium oleate with β-lactoglobulin*. European Journal of Lipid Science and Technology 113 1207-1218.

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Lišková *et al.* (2010) *Effect of α-lactalbumin denaturation on its potential anti-cancer properties*. Journal of Agricultural and Food Chemistry 58(7) 4421-4427.

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