

## Dietary vitamin D, a powerful weapon in the war against colorectal cancer

### Abstract

Epidemiological, experimental, and animal studies indicate that theoretically, at least 50% of sporadic colorectal cancer cases could be prevented by modifications of dietary habits. In spite of the already significant amount of evidence, there is still reluctance to accept that diet has a fundamental role in colon tumourigenesis, due to poor understanding of the mechanisms that regulate this process. The risk of developing colorectal cancer is dramatically increased in patients with inflammatory bowel disease (IBD). Diet has a strong impact on development, severity and outcome of both colorectal cancer and IBD. Calcitriol (1,25-dihydroxyvitamin D<sub>3</sub>; 1,25-D<sub>3</sub>), the most active metabolite of vitamin D has anti-proliferative, anti-angiogenic, pro-differentiating, and pro-apoptotic actions. Evidence is increasing that high tissue-levels of 1,25-D<sub>3</sub> synthesized in the organs prone to sporadic cancers counteract incipient neoplasia.

We propose to investigate the relationship between a western-type stress diet and inflammation-associated colon cancer. We plan to establish whether vitamin D could be used as a chemopreventive agent against colorectal cancer and inflammatory bowel disease.

First we will test if the so-called New Western Diet, a nutritional stress diet, that mimics the intake levels of nutrients that are recognised as major dietary risk factors for human colorectal cancer, will accelerate tumourigenesis and aggravate the symptoms in the inflammation-associated colon cancer model.

Then we will examine whether high vitamin D intake is able to ameliorate the severity of inflammation and prevent, or delay malignant transformation. In a second experiment we propose to test in a colorectal cancer xenograft model whether overexpressing the enzyme that catabolises the active vitamin D metabolite (24-hydroxylase; CYP24A1) in the tumour, enhances local 1,25-D<sub>3</sub> degradation, causing resistance to vitamin D and whether dietary soy can restore responsiveness to calcitriol by inhibiting CYP24A1 activity.

The proposed study will establish whether dietary vitamin D is a potent and reliable chemopreventive agent that is able to reduce the impact of a Western-type nutritional stress diet in colon tumourigenesis. Then we will show whether vitamin D, as a potent immune modulator, is able to delay, prevent relapse, or ameliorate symptoms of IBD.

Furthermore, we will be able to demonstrate unequivocally the impact of local CYP24A1 overexpression on vitamin D signalling and growth potential of the tumour and whether this can be inhibited by a phytoestrogen-rich diet.

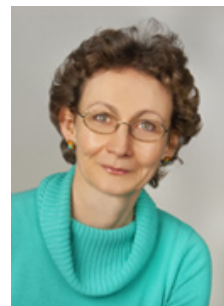
Our study will demonstrate whether a risk diet indeed increases inflammation-associated colorectal carcinogenesis. It will verify whether increasing vitamin D intake would reduce the risk of developing cancer, identifying a cheap and simple chemoprevention strategy. Thus we will provide additional evidence to increase awareness in the population for the importance of a balanced diet.

Keywords:

New Western Diet, vitamin D, soy, tumour xenograft, CYP24A1

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Further links about the involved persons and regarding the project you can find at  
[https://archiv.wtlf.at/programmes/life\\_sciences/LS12-047](https://archiv.wtlf.at/programmes/life_sciences/LS12-047)