



Professor Margreet Visser

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Principal Investigator
Associate Dean (Research)

BSc(Hons)(Cant) MSc PhD(Otago)

Email margreet.vissers@otago.ac.nz

Tel +64 3 364 1524



Research interests

Vitamin C and cancer

Most of my current research revolves around determining the biological functions of vitamin C (ascorbate), which is widely considered to be an important natural antioxidant. However, ascorbate is also an essential co-factor for a family of enzymes, the 2-oxoglutarate-dependent dioxygenases, which control many biological processes, ranging from the stress response to hypoxia, to the regulation of epigenetic enzymes. These processes are important in cancer and we are investigating the contribution of ascorbate to cancer growth as a result of its co-factor activity for these enzymes. We are planning clinical trials to determine the impact of ascorbate on the processes involved in cancer cell biology.

Vitamin C and immunity

The cofactor activities of ascorbate are likely to influence many biological processes that impact on health and disease, and our aim is to understand the extent of this involvement in the functioning of the immune system. My research has shown that ascorbate affects white blood cell function, and we have an interest in the role of ascorbate in acute inflammatory diseases such as pneumonia and sepsis.

Vitamin C and optimal health

We have investigated the comparative bioavailability of vitamin C from different sources (i.e. food-derived or synthetic) to organs and tissues in an animal model and human subjects. This research will help to inform the debate around the appropriate Nutrient Reference Value and Recommended Dietary Intake for vitamin C. Ascorbate acts as a cofactor for the enzymatic synthesis of mood and energy controlling hormones. We have investigated the association of vitamin C intake from an excellent food source (kiwifruit) with measures of subjective mood, including fatigue, and shown that a high vitamin C diet can improve mood and energy levels. This preliminary research will be followed up with a larger clinical study.

White blood cells and inflammation

My research interests also include the investigation of cellular responses to stress, in particular stress resulting from exposure to oxidants. I have extensive experience in working with inflammatory cells, particularly neutrophils, as a source of highly reactive oxidants. Neutrophils generate hypochlorous acid (HOCl), i.e. household bleach, which is known for its anti-microbial activity. HOCl

also reacts with many biological targets, as we are investigating how it damages cells and tissues, and how it contributes to the many deleterious effects of chronic inflammatory diseases such as atherosclerosis. The oxidative stress-related processes we are most interested in are apoptosis (cell clearance from sites of inflammation), cell signalling (e.g. nuclear factor- κ B; NF κ B, and hypoxia-inducible factor 1 α ; HIF-1) and cytotoxicity (cell death).

Keywords: cancer, immunity, vitamin C (ascorbate), inflammation, atherosclerosis, oxidative stress, antioxidants.

In the media

Professor Margreet Vissers was featured in Radio New Zealand's The Science Of... Vitamin C in August 2017.

Publications

Film/Video/CD Rom

Fraser, R., Chambers, S., Fellows, A., Brennan, S., Vissers, M., Fu, R., & Scott-Thomas, A. (2009). The Body, the Research, the Professor: Respiratory Research and Cystic Fibrosis [Episode 5] [Film]. Christchurch, New Zealand: Canterbury Medical Research Foundation. Retrieved from <http://www.cmrf.org.nz/Home/Videos/#vid1>

Chapter in Book - Research

Vissers, M. C. M., Carr, A. C., Pullar, J. M., & Bozonet, S. M. (2013). The bioavailability of vitamin C from kiwifruit. In M. Boland & P. J. Moughan (Eds.), *Nutritional benefits of kiwifruit*. (pp. 125-147). Waltham, MA: Academic Press. doi: 10.1016/b978-0-12-394294-4.00007-9

Journal - Research Article

Campbell, E. J., Vissers, M. C. M., Bozonet, S., Dyer, A., Robinson, B. A., & Dachs, G. U. (2015). Restoring physiological levels of ascorbate slows tumor growth and moderates HIF-1 pathway activity in *Gulo*^{-/-} mice. *Cancer Medicine*, 4(2), 303-314. doi: 10.1002/cam4.349

Wilkie-Grantham, R. P., Magon, N. J., Harwood, D. T., Kettle, A. J., Vissers, M. C., Winterbourn, C. C., & Hampton, M. B. (2015). Myeloperoxidase-dependent lipid peroxidation promotes the oxidative modification of cytosolic proteins in phagocytic neutrophils. *Journal of Biological Chemistry*, 290(15), 9896-9905. doi: 10.1074/jbc.M114.613422

Bozonet, S. M., Carr, A. C., Pullar, J. M., & Vissers, M. C. M. (2015). Enhanced human neutrophil vitamin C status, chemotaxis and oxidant generation following dietary supplementation with vitamin C-rich *SunGold* kiwifruit. *Nutrients*, 7(4), 2574-2588. doi: 10.3390/nu7042574

Flett, T., Campbell, E. J., Phillips, E., Vissers, M. C. M., & Dachs, G. U. (2014). Gulonolactone addition to human hepatocellular carcinoma cells with gene transfer of gulonolactone oxidase restores ascorbate biosynthesis and reduces hypoxia inducible factor 1. *Biomedicines*, 2(1), 98-109. doi: 10.3390/biomedicines2010098

Kuiper, C., & Vissers, M. C. M. (2014). Ascorbate as a cofactor for Fe- and 2-oxoglutarate dependent dioxygenases: Physiological activity in tumour growth and progression. *Frontiers in Oncology*, 4, 359. doi: 10.3389/fonc.2014.00359

Vissers, M. C. M., Kuiper, C., & Dachs, G. U. (2014). Regulation of the 2-oxoglutarate-dependent dioxygenases and implications for cancer. *Biochemical Society Transactions*, 42(4), 945-951. doi: 10.1042/bst20140118

Kuiper, C., Vissers, M. C. M., & Hicks, K. O. (2014). Pharmacokinetic modelling of ascorbate diffusion through normal and tumour tissue. *Free Radical Biology & Medicine*, 77, 340-352. doi: 10.1016/j.freeradbiomed.2014.09.023

Kuiper, C., Dachs, G. U., Currie, M. J., & Vissers, M. C. M. (2014). Intracellular ascorbate enhances hypoxia-inducible factor (HIF)-hydroxylase activity and preferentially suppresses the HIF-1 transcriptional response. *Free Radical Biology & Medicine*, 69, 308-317. doi: 10.1016/j.freeradbiomed.2014.01.033

Carr, A. C., Vissers, M. C. M., & Cook, J. S. (2014). The effect of intravenous vitamin C on cancer- and chemotherapy-related fatigue and quality of life. *Frontiers in Oncology*, 4, 283. doi: 10.3389/fonc.2014.00283

- Kuiper, C., Dachs, G. U., Munn, D., Currie, M. J., Robinson, B. A., Pearson, J. F., & Vissers, M. C. M. (2014). Increased tumour ascorbate is associated with extended disease-free survival and decreased hypoxia-inducible factor-1 activation in human colorectal cancer. *Frontiers in Oncology*, 4, 10. doi: 10.3389/fonc.2014.00010
- Carr, A. C., Bozonet, S. M., Pullar, J. M., & Vissers, M. C. M. (2013). Mood improvement in young adult males following supplementation with gold kiwifruit, a high-vitamin C food. *Journal of Nutritional Science*, 2, e24. doi: 10.1017/jns.2013.12
- Carr, A. C., Bozonet, S. M., Pullar, J. M., Simcock, J. W., & Vissers, M. C. M. (2013). A randomized steady-state bioavailability study of synthetic versus natural (kiwifruit-derived) vitamin C. *Nutrients*, 5(9), 3684-3695. doi: 10.3390/nu5093684
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- Parker, A., Cuddihy, S. L., Son, T. G., Vissers, M. C. M., & Winterbourn, C. C. (2011). Roles of superoxide and myeloperoxidase in ascorbate oxidation in stimulated neutrophils and H₂O₂-treated HL60 cells. *Free Radical Biology & Medicine*, 51(7), 1399-1405. doi: 10.1016/j.freeradbiomed.2011.06.029
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- Kuiper, C., Molenaar, I. G. M., Dachs, G. U., Currie, M. J., Sykes, P. H., & Vissers, M. C. M. (2010). Low ascorbate levels are associated with increased hypoxia-inducible factor-1 activity and an aggressive tumor phenotype in endometrial cancer. *Cancer Research*, 70(14), 5749-5758. doi: 10.1158/0008-5472.CAN-10-0263
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Journal - Research Other

- Carr, A. C., Vissers, M. C. M., & Cook, J. S. (2015). Parenteral vitamin C relieves chronic fatigue and pain in a patient with rheumatoid arthritis and mononeuritis multiplex secondary to CNS vasculitis. *Case Reports in Clinical Pathology*, 2(2), 57-61. doi: 10.5430/crcp.v2n2p57

Conference Contribution - Verbal presentation and other Conference outputs

Vissers, M. (2014, July). *Cell metabolism and control of the 2-oxoglutarate-dependent dioxygenases*. Verbal presentation at the Oxygen Theme Meeting, Christchurch, New Zealand.

Vissers, M. C. M., & Kuiper, C. (2014, August). *Regulation of the 2-oxoglutarate-dependent dioxygenases and implications for cancer*. Verbal presentation at the Queenstown Molecular Biology (QMB) Meetings, Queenstown, New Zealand.

Vissers, M. (2014, August). *Metabolic sensing by the 2-oxoglutarate-dependent dioxygenase demethylases and potential effects on epigenetics*. Verbal presentation at the Queenstown Molecular Biology (QMB) Meetings, Queenstown, New Zealand.

Vissers, M. (2009, December). *Inhibition of apoptosis and caspase 3 activation in endothelial cells by hypothiocyanous acid*. Verbal presentation at the 5th Joint Meeting of The Societies for Free Radical Research Australasia and Japan & Mutagenesis and Experimental Pathology Society of Australia, Sydney, Australia.

Vissers, M., & Kuiper, C. (2009, November). *Vitamin C and the regulation of HIF-1: Impact on cell survival in inflammation and cancer*. Plenary presentation at the Society for Free Radical Biology and Medicine (SFRBM) 16th Annual Meeting, San Francisco, CA, USA.

Fewer publications...