

Erasmus University Rotterdam, the Netherlands
CSC PhD 2015 Project Description

School/Department:	Department of Internal Medicine, Endocrinology
Project Title:	The search for the unacylated ghrelin receptor
Abstract:	<p>Our laboratory has been working on the cellular and metabolic effects of the unacylated form of ghrelin. Ghrelin is a 28-amino acid peptide made in the stomach and occurs in two forms, acylated ghrelin that is modified with octanoyl acid (AG) and unacylated ghrelin (UAG) which does not have this fatty acid modification. AG acts on the growth hormone secretagogue receptor (GHSR) to produce its effects and potently causes feelings of hunger and experimental treatment with AG causes obesity and insulin resistance. Intriguingly, we and other groups have found that unacylated ghrelin (UAG) might counteract these bad effects of AG on metabolism. We are now testing a short analogue of UAG in phase I clinical trials to discover if it can reverse the effects of obesity and/or diabetes. However, despite evidence for biological activity of UAG on various cell types and in animals and humans, and that inhibition of a range of signaling pathways block its activity, we still do not know its precise mechanism of action. This project is aimed at discovering a receptor for UAG.</p>
Requirements of candidate:	<p>Master degree: Yes</p> <p>Background: Experience with basic laboratory techniques (pipetting, preparation of experimental solutions, etc.). Molecular biological techniques (eg. agarose gel preparation, PCR), as well as bacterial and mammalian cell culture are important parts of the project and experience with these techniques would be an advantage.</p> <p>IELTS Grade: 7.0 (<i>minimal 6.0 per component</i>) or TOEFL: 100 (<i>minimal 20 per component</i>)</p>
Supervisor information:	<p>Dr. Patric Delhanty Email: p.delhanty@erasmusmc.nl</p> <p>Recent publication list</p> <ol style="list-style-type: none"> Stevanovic DM, Grefhorst A, Themmen AP, Popovic V, Holstege J, Haasdijk E, Trajkovic V, van der Lely AJ,

	<p>Delhanty PJ. Unacylated ghrelin suppresses ghrelin-induced neuronal activity in the hypothalamus and brainstem of male rats. <i>PLoS One</i>. 2014;9(5):e98180.</p> <p>2. Ozcan B, Neggers SJ, Miller AR, Yang HC, Lucaites V, Abribat T, Allas S, Huisman M, Visser JA, Themmen AP, Sijbrands E, Delhanty P, Van der Lely AJ. Does des-acyl ghrelin improve glycemic control in obese diabetic subjects by decreasing acylated ghrelin levels? <i>Eur J Endocrinol</i>. 2014;170(6):799-807.</p> <p>3. Fani L, Bak S, Delhanty P, van Rossum EF, van den Akker EL. The melanocortin-4 receptor as target for obesity treatment: a systematic review of emerging pharmacological therapeutic options. <i>Int J Obes (Lond)</i>. 2014;38(2):163-169.</p> <p>4. Delhanty PJ, van der Velde M, van der Eerden BC, Sun Y, Geminn JM, der Lely AJ, Smith RG, van Leeuwen JP. Genetic manipulation of the ghrelin signaling system in male mice reveals bone compartment specificity of acylated and unacylated ghrelin in the regulation of bone remodeling. <i>Endocrinology</i>. 2014:en20132055.</p> <p>5. Delhanty PJ, van der Eerden BC, van Leeuwen JP. Ghrelin and bone. <i>Biofactors</i>. 2014;40(1):41-48.</p> <p>6. Delhanty PJ, Neggers SJ, van der Lely AJ. Should we consider des-acyl ghrelin as a separate hormone and if so, what does it do? <i>Front Horm Res</i>. 2014;42:163-174.</p> <p>7. Delhanty PJ, Huisman M, Julien M, Mouchain K, Brune P, Themmen A, Abribat T, van der Lely A. The acylated (AG) to unacylated (UAG) ghrelin ratio in esterase inhibitor treated blood is higher than previously described. <i>Clin Endocrinol (Oxf)</i>. 2014;10.1111/cen.12489.</p> <p>8. Bouw E, Huisman M, Neggers SJ, Themmen AP, van der Lely AJ, Delhanty PJ. Development of potent selective competitive-antagonists of the melanocortin type 2 receptor. <i>Mol Cell Endocrinol</i>. 2014;394(1-2):99-104.</p> <p>9. Delhanty PJ, Neggers SJ, van der Lely AJ. Des-acyl ghrelin: a metabolically active Peptide. <i>Endocr Dev</i>. 2013;25:112-121.</p> <p>10. Delhanty PJ, Huisman M, Baldeon-Rojas LY, van den Berge I, Grefhorst A, Abribat T, Leenen PJ, Themmen AP, van der Lely AJ. Des-acyl ghrelin analogs prevent high-fat-diet-induced dysregulation of glucose homeostasis. <i>FASEB J</i>. 2013;27:1690-1700.</p> <p>11. van der Velde M, van der Eerden BCJ, Sun Y, Almering JMM, van der Lely A-J, Delhanty PJD, Smith RG, van</p>
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	<p>Leeuwen JPTM. An Age-Dependent Interaction with Leptin Unmasks Ghrelin's Bone-Protective Effects. <i>Endocrinology</i>. 2012;153(8):3593-3602.</p> <p>12. Julien M, Kay RG, Delhanty PJ, Allas S, Granata R, Barton C, Constable S, Ghigo E, van der Lely AJ, Abribat T. In vitro and in vivo stability and pharmacokinetic profile of unacylated ghrelin (UAG) analogues. <i>Eur J Pharm Sci</i>. 2012;47(4):625-635.</p> <p>13. Hofland J, Delhanty PJ, Steenbergen J, Hofland LJ, van Koetsveld PM, van Nederveen FH, de Herder WW, Feelders RA, de Jong FH. Melanocortin 2 Receptor-Associated Protein (MRAP) and MRAP2 in Human Adrenocortical Tissues: Regulation of Expression and Association with ACTH Responsiveness. <i>J Clin Endocrinol Metab</i>. 2012;10.1210/jc.2011-2328.</p> <p>14. Delhanty PJ, van der Lely AJ. Ghrelin: a new treatment for non-alcoholic fatty liver disease? <i>Endocrine</i>. 2012.</p> <p>15. Delhanty PJ, Neggers SJ, Van der Lely AJ. Ghrelin: The Differences between Acyl- and Des-acyl Ghrelin. <i>Eur J Endocrinol</i>. 2012;167:601-608.</p> <p>16. Blijdorp K, van den Heuvel-Eibrink MM, Pieters R, Boot AM, Delhanty PJ, van der Lely AJ, Neggers SJ. Obesity is underestimated using body mass index and waist-hip ratio in long-term adult survivors of childhood cancer. <i>PLoS One</i>. 2012;7(8):e43269.</p> <p>17. Delhanty PJ, van der Lely AJ. Ghrelin and glucose homeostasis. <i>Peptides</i>. 2011;32(11):2309-2318.</p>
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