

1. Eerola, K.; Virtanen, S.; Vahatalo, L.; Ailanen, L.; Cai, M.; Hruby, V.; Savontaus, M.; Savontaus, E., Hypothalamic gamma-melanocyte stimulating hormone gene delivery reduces fat mass in male mice. *J Endocrinol* **2018**.
2. Mowlazadeh Haghghi, S.; Zhou, Y.; Dai, J.; Sawyer, J. R.; Hruby, V. J.; Cai, M., Replacement of Arg with Nle and modified D-Phe in the core sequence of MSHs, Ac-His-D-Phe-Arg-Trp-NH₂, leads to hMC1R selectivity and pigmentation. *Eur J Med Chem* **2018**, *151*, 815-823.
3. Merlino, F.; Zhou, Y.; Cai, M.; Carotenuto, A.; Yousif, A. M.; Brancaccio, D.; Di Maro, S.; Zappavigna, S.; Limatola, A.; Novellino, E.; Grieco, P.; Hruby, V. J., Development of Macroyclic Peptidomimetics Containing Constrained alpha,alpha-Dialkylated Amino Acids with Potent and Selective Activity at Human Melanocortin Receptors. *J Med Chem* **2018**, *61* (9), 4263-4269.
4. Durek, T.; Cromm, P. M.; White, A. M.; Schroeder, C. I.; Kaas, Q.; Weidmann, J.; Ahmad Fuaad, A.; Cheneval, O.; Harvey, P. J.; Daly, N. L.; Zhou, Y.; Dellsen, A.; Osterlund, T.; Larsson, N.; Knerr, L.; Bauer, U.; Kessler, H.; Cai, M.; Hruby, V. J.; Plowright, A. T.; Craik, D. J., Development of Novel Melanocortin Receptor Agonists Based on the Cyclic Peptide Framework of Sunflower Trypsin Inhibitor-1. *J Med Chem* **2018**, *61* (8), 3674-3684.
5. Zhou, Y.; Mowlazadeh Haghghi, S.; Zoi, I.; Sawyer, J. R.; Hruby, V. J.; Cai, M., Design of MC1R Selective gamma-MSH Analogues with Canonical Amino Acids Leads to Potency and Pigmentation. *J Med Chem* **2017**, *60* (22), 9320-9329.
6. Cai, M.; Marelli, U. K.; Mertz, B.; Beck, J. G.; Opperer, F.; Rechenmacher, F.; Kessler, H.; Hruby, V. J., Structural Insights into Selective Ligand-Receptor Interactions Leading to Receptor Inactivation Utilizing Selective Melanocortin 3 Receptor Antagonists. *Biochemistry-US* **2017**, *56* (32), 4201-4209.
7. Zhou, Y.; Cai, M., Novel approaches to the design of bioavailable melanotropins. *Expert Opin Drug Discov* **2017**, *12* (10), 1023-1030.
8. Rinne, P.; Rami, M.; Nuutinen, S.; Santovito, D.; van der Vorst, E. P. C.; Guillamat-Prats, R.; Lyytikainen, L. P.; Raitoharju, E.; Oksala, N.; Ring, L.; Cai, M.; Hruby, V. J.; Lehtimaki, T.; Weber, C.; Steffens, S., Melanocortin 1 Receptor Signaling Regulates Cholesterol Transport in Macrophages. *Circulation* **2017**, *136* (1), 83-97.
9. Cai, M.; Hruby, V. J., Design of cyclized selective melanotropins. *Biopolymers* **2016**, *106* (6), 876-883.
10. Cai, M.; Hruby, V. J., The Melanocortin Receptor System: A Target for Multiple Degenerative Diseases. *Curr Protein Pept Sci* **2016**, *17* (5), 488-96.
11. Carotenuto, A.; Merlino, F.; Cai, M.; Brancaccio, D.; Yousif, A. M.; Novellino, E.; Hruby, V. J.; Grieco, P., Discovery of Novel Potent and Selective Agonists at the Melanocortin-3 Receptor. *J Med Chem* **2015**, *58* (24), 9773-8.
12. Shukla, C.; Koch, L. G.; Britton, S. L.; Cai, M.; Hruby, V. J.; Bednarek, M.; Novak, C. M., Contribution of regional brain melanocortin receptor subtypes to elevated activity energy expenditure in lean, active rats. *Neuroscience* **2015**, *310*, 252-67.
13. Cai, M.; Marelli, U. K.; Bao, J.; Beck, J. G.; Opperer, F.; Rechenmacher, F.; McLeod, K. R.; Zingsheim, M. R.; Doedens, L.; Kessler, H.; Hruby, V. J., Systematic Backbone Conformational Constraints on a Cyclic Melanotropin Ligand Leads to Highly Selective Ligands for Multiple Melanocortin Receptors. *J Med Chem* **2015**, *58* (16), 6359-67.
14. Van der Poorten, O.; Feher, K.; Buysse, K.; Feytens, D.; Zoi, I.; Schwartz, S. D.; Martins, J. C.; Tourwe, D.; Cai, M.; Hruby, V. J.; Ballet, S., Azepinone-Containing Tetrapeptide Analogues of Melanotropin Lead to Selective hMC4R Agonists and hMC5R Antagonist. *AcS Med Chem Lett* **2015**, *6* (2), 192-7.
15. Cai, M.; Stankova, M.; Muthu, D.; Mayorov, A.; Yang, Z.; Trivedi, D.; Cabello, C.; Hruby, V. J., An unusual conformation of gamma-melanocyte-stimulating hormone analogues leads to a selective human melanocortin 1 receptor antagonist for targeting melanoma cells. *Biochemistry-US* **2013**, *52* (4), 752-64.
16. Rinne, P.; Nordlund, W.; Heinonen, I.; Penttinen, A. M.; Saraste, A.; Ruohonen, S. T.; Makela, S.; Vahatalo, L.; Kaipio, K.; Cai, M.; Hruby, V. J.; Ruohonen, S.; Savontaus, E., alpha-Melanocyte-

- stimulating hormone regulates vascular NO availability and protects against endothelial dysfunction. *Cardiovasc Res* **2013**, *97* (2), 360-8.
- 17. Hruby, V. J.; Cai, M.; Nyberg, J.; Muthu, D., Approaches to the rational design of selective melanocortin receptor antagonists. *Expert Opin Drug Discov* **2011**, *6* (5), 543-57.
 - 18. Mayorov, A. V.; Cai, M.; Palmer, E. S.; Tanaka, D. K.; Cain, J. P.; Dedek, M. M.; Tan, B.; Trivedi, D.; Hruby, V. J., Cyclic lactam hybrid alpha-MSH/Agouti-related protein (AGRP) analogues with nanomolar range binding affinities at the human melanocortin receptors. *Bioorg Med Chem Lett* **2011**, *21* (10), 3099-102.
 - 19. Cai, M.; Liu, Z.; Qu, H.; Fan, H.; Zheng, Z.; Hruby, V. J., Utilize conjugated melanotropins for the earlier diagnosis and treatment of melanoma. *Eur J Pharmacol* **2011**, *660* (1), 188-93.
 - 20. Hruby, V. J.; Cai, M.; Cain, J.; Nyberg, J.; Trivedi, D., Design of novel melanocortin receptor ligands: multiple receptors, complex pharmacology, the challenge. *Eur J Pharmacol* **2011**, *660* (1), 88-93.
 - 21. Mayorov, A. V.; Cai, M.; Palmer, E. S.; Liu, Z.; Cain, J. P.; Vagner, J.; Trivedi, D.; Hruby, V. J., Solid-phase peptide head-to-side chain cyclodimerization: discovery of C(2)-symmetric cyclic lactam hybrid alpha-melanocyte-stimulating hormone (MSH)/agouti-signaling protein (ASIP) analogues with potent activities at the human melanocortin receptors. *Peptides* **2010**, *31* (10), 1894-905.
 - 22. Doedens, L.; Opperer, F.; Cai, M.; Beck, J. G.; Dedek, M.; Palmer, E.; Hruby, V. J.; Kessler, H., Multiple N-methylation of MT-II backbone amide bonds leads to melanocortin receptor subtype hMC1R selectivity: pharmacological and conformational studies. *J Am Chem Soc* **2010**, *132* (23), 8115-28.
 - 23. Juni, A.; Cai, M.; Stankova, M.; Waxman, A. R.; Arout, C.; Klein, G.; Dahan, A.; Hruby, V. J.; Mogil, J. S.; Kest, B., Sex-specific mediation of opioid-induced hyperalgesia by the melanocortin-1 receptor. *Anesthesiology* **2010**, *112* (1), 181-8.
 - 24. Yang, Y.; Hruby, V. J.; Chen, M.; Crasto, C.; Cai, M.; Harmon, C. M., Novel binding motif of ACTH analogues at the melanocortin receptors. *Biochemistry-US* **2009**, *48* (41), 9775-84.
 - 25. Cai, M.; Nyberg, J.; Hruby, V. J., Melanotropins as drugs for the treatment of obesity and other feeding disorders: potential and problems. *Curr Top Med Chem* **2009**, *9* (6), 554-63.
 - 26. Qu, H.; Cai, M.; Mayorov, A. V.; Grieco, P.; Zingsheim, M.; Trivedi, D.; Hruby, V. J., Substitution of arginine with proline and proline derivatives in melanocyte-stimulating hormones leads to selectivity for human melanocortin 4 receptor. *J Med Chem* **2009**, *52* (12), 3627-35.
 - 27. Hruby, V. J.; Cai, M.; Dedek, M.; Qu, H.; Palmer, E.; Mayorov, A.; Trivedi, D.; Tsaprailis, G.; Yang, Y., Peptide and non-peptide mimetics utilize different pathways for signal transduction. *Adv Exp Med Biol* **2009**, *611*, 305-7.
 - 28. Min, B. J.; Mayorov, A. V.; Cai, M.; Palmer, E.; Hruby, V. J., Design and parallel synthesis of new bicyclic small molecules for targeting the melanocortin receptors. *Adv Exp Med Biol* **2009**, *611*, 187-8.
 - 29. Yang, Y.; Cai, M.; Chen, M.; Qu, H.; McPherson, D.; Hruby, V.; Harmon, C. M., Key amino acid residues in the melanocortin-4 receptor for nonpeptide THIQ specific binding and signaling. *Regul Pept* **2009**, *155* (1-3), 46-54.
 - 30. Chen, M.; Cai, M.; McPherson, D.; Hruby, V.; Harmon, C. M.; Yang, Y., Contribution of the transmembrane domain 6 of melanocortin-4 receptor to peptide [Pro5, DNal (2')8]-gamma-MSH selectivity. *Biochem Pharmacol* **2009**, *77* (1), 114-24.
 - 31. Grieco, P.; Cai, M.; Liu, L.; Mayorov, A.; Chandler, K.; Trivedi, D.; Lin, G.; Campiglia, P.; Novellino, E.; Hruby, V. J., Design and microwave-assisted synthesis of novel macrocyclic peptides active at melanocortin receptors: discovery of potent and selective hMC5R receptor antagonists. *J Med Chem* **2008**, *51* (9), 2701-7.
 - 32. Lee, M.; Kim, A.; Conwell, I. M.; Hruby, V.; Mayorov, A.; Cai, M.; Wardlaw, S. L., Effects of selective modulation of the central melanocortin-3-receptor on food intake and hypothalamic POMC expression. *Peptides* **2008**, *29* (3), 440-7.
 - 33. Mayorov, A. V.; Cai, M.; Palmer, E. S.; Dedek, M. M.; Cain, J. P.; Van Scy, A. R.; Tan, B.; Vagner, J.; Trivedi, D.; Hruby, V. J., Structure-activity relationships of cyclic lactam analogues of alpha-

- melanocyte-stimulating hormone (alpha-MSH) targeting the human melanocortin-3 receptor. *J Med Chem* **2008**, *51* (2), 187-95.
- 34. Lee, Y. S.; Agnes, R. S.; Cain, J. P.; Kulkarni, V.; Cai, M.; Salibay, C.; Ciano, K.; Petrov, R.; Mayorov, A.; Vagner, J.; Trivedi, D.; Davis, P.; Ma, S. W.; Lai, J.; Porreca, F.; Vardanyan, R.; Hruby, V. J., Opioid and melanocortin receptors: do they have overlapping pharmacophores? *Biopolymers* **2008**, *90* (3), 433-8.
 - 35. Hruby, V. J.; Cai, M.; Cain, J. P.; Mayorov, A. V.; Dedek, M. M.; Trivedi, D., Design, synthesis and biological evaluation of ligands selective for the melanocortin-3 receptor. *Curr Top Med Chem* **2007**, *7* (11), 1107-19.
 - 36. Chen, M.; Cai, M.; Aprahamian, C. J.; Georgeson, K. E.; Hruby, V.; Harmon, C. M.; Yang, Y., Contribution of the conserved amino acids of the melanocortin-4 receptor in [corrected] [Nle⁴,D-Phe⁷]-alpha-melanocyte-stimulating [corrected] hormone binding and signaling. *J Biol Chem* **2007**, *282* (30), 21712-9.
 - 37. Grieco, P.; Cai, M.; Han, G.; Trivedi, D.; Campiglia, P.; Novellino, E.; Hruby, V. J., Further structure-activity studies of lactam derivatives of MT-II and SHU-9119: their activity and selectivity at human melanocortin receptors 3, 4, and 5. *Peptides* **2007**, *28* (6), 1191-6.
 - 38. Ballet, S.; Mayorov, A. V.; Cai, M.; Tymecka, D.; Chandler, K. B.; Palmer, E. S.; Rompaey, K. V.; Misicka, A.; Tourwe, D.; Hruby, V. J., Novel selective human melanocortin-3 receptor ligands: use of the 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba) scaffold. *Bioorg Med Chem Lett* **2007**, *17* (9), 2492-8.
 - 39. Ying, J.; Gu, X.; Cai, M.; Dedek, M.; Vagner, J.; Trivedi, D. B.; Hruby, V. J., Design, synthesis, and biological evaluation of new cyclic melanotropin peptide analogues selective for the human melanocortin-4 receptor. *J Med Chem* **2006**, *49* (23), 6888-96.
 - 40. Cai, M.; Varga, E. V.; Stankova, M.; Mayorov, A.; Perry, J. W.; Yamamura, H. I.; Trivedi, D.; Hruby, V. J., Cell signaling and trafficking of human melanocortin receptors in real time using two-photon fluorescence and confocal laser microscopy: differentiation of agonists and antagonists. *Chem Biol Drug Des* **2006**, *68* (4), 183-93.
 - 41. Cain, J. P.; Mayorov, A. V.; Cai, M.; Wang, H.; Tan, B.; Chandler, K.; Lee, Y.; Petrov, R. R.; Trivedi, D.; Hruby, V. J., Design, synthesis, and biological evaluation of a new class of small molecule peptide mimetics targeting the melanocortin receptors. *Bioorg Med Chem Lett* **2006**, *16* (20), 5462-7.
 - 42. Mayorov, A. V.; Han, S. Y.; Cai, M.; Hammer, M. R.; Trivedi, D.; Hruby, V. J., Effects of macrocycle size and rigidity on melanocortin receptor-1 and -5 selectivity in cyclic lactam alpha-melanocyte-stimulating hormone analogs. *Chem Biol Drug Des* **2006**, *67* (5), 329-35.
 - 43. Mayorov, A. V.; Cai, M.; Chandler, K. B.; Petrov, R. R.; Van Scy, A. R.; Yu, Z.; Tanaka, D. K.; Trivedi, D.; Hruby, V. J., Development of cyclic gamma-MSH analogues with selective hMC3R agonist and hMC3R/hMC5R antagonist activities. *J Med Chem* **2006**, *49* (6), 1946-52.
 - 44. Grieco, P.; Cai, M.; Mayorov, A. V.; Trivedi, D.; Hruby, V. J., Structure-activity studies of new melanocortin peptides containing an aromatic amino acid at the N-terminal position. *Peptides* **2006**, *27* (2), 472-81.
 - 45. Cai, M.; Mayorov, A. V.; Ying, J.; Stankova, M.; Trivedi, D.; Cabello, C.; Hruby, V. J., Design of novel melanotropin agonists and antagonists with high potency and selectivity for human melanocortin receptors. *Peptides* **2005**, *26* (8), 1481-5.
 - 46. Cai, M.; Mayorov, A. V.; Cabello, C.; Stankova, M.; Trivedi, D.; Hruby, V. J., Novel 3D pharmacophore of alpha-MSH/gamma-MSH hybrids leads to selective human MC1R and MC3R analogues. *J Med Chem* **2005**, *48* (6), 1839-48.
 - 47. Cai, M.; Stankova, M.; Pond, S. J.; Mayorov, A. V.; Perry, J. W.; Yamamura, H. I.; Trivedi, D.; Hruby, V. J., Real time differentiation of G-protein coupled receptor (GPCR) agonist and antagonist by two photon fluorescence laser microscopy. *J Am Chem Soc* **2004**, *126* (23), 7160-1.
 - 48. Cai, M.; Cai, C.; Mayorov, A. V.; Xiong, C.; Cabello, C. M.; Soloshonok, V. A.; Swift, J. R.; Trivedi, D.; Hruby, V. J., Biological and conformational study of beta-substituted prolines in MT-II template: steric effects leading to human MC5 receptor selectivity. *J Pept Res* **2004**, *63* (2), 116-31.

49. Balse-Srinivasan, P.; Grieco, P.; Cai, M.; Trivedi, D.; Hruby, V. J., Structure-activity relationships of gamma-MSH analogues at the human melanocortin MC3, MC4, and MC5 receptors. Discovery of highly selective hMC3R, hMC4R, and hMC5R analogues. *J Med Chem* **2003**, *46* (23), 4965-73.
50. Balse-Srinivasan, P.; Grieco, P.; Cai, M.; Trivedi, D.; Hruby, V. J., Structure-activity relationships of novel cyclic alpha-MSH/beta-MSH hybrid analogues that lead to potent and selective ligands for the human MC3R and human MC5R. *J Med Chem* **2003**, *46* (17), 3728-33.
51. Hruby, V. J.; Cai, M.; Grieco, P.; Han, G.; Kavarana, M.; Trivedi, D., Exploring the stereostructural requirements of peptide ligands for the melanocortin receptors. *Ann N Y Acad Sci* **2003**, *994*, 12-20.
52. Grieco, P.; Lavecchia, A.; Cai, M.; Trivedi, D.; Weinberg, D.; MacNeil, T.; Van der Ploeg, L. H.; Hruby, V. J., Structure-activity studies of the melanocortin peptides: discovery of potent and selective affinity antagonists for the hMC3 and hMC4 receptors. *J Med Chem* **2002**, *45* (24), 5287-94.
53. Kavarana, M. J.; Trivedi, D.; Cai, M.; Ying, J.; Hammer, M.; Cabello, C.; Grieco, P.; Han, G.; Hruby, V. J., Novel cyclic templates of alpha-MSH give highly selective and potent antagonists/agonists for human melanocortin-3/4 receptors. *J Med Chem* **2002**, *45* (12), 2644-50.