Scientific Research on Beta-Caseins

This site serves to provide a comprehensive and up-to-date resource of published scientific literature relating to the major milk proteins beta-casein A1 and A2 and human health.

There are over 80 internationally published and peer reviewed studies that address different aspects of science relating to the the beta-casein variants and casomorphin-7(BCM-7), a bioactive protein fragment preferentially derived from A1 during digestion.

The relevant literature spans the areas of type 1 diabetes, heart disease, autism, as well as a range of biological responses that BCM-7 has the potential to elicit on a range of tissues and cells.

The literature comprises research that encompass epidemiology, biochemistry, immunology, human and animal studies, pharmacology and genetics.

REVIEW ARTICLES RELATING TO BETA-CASEIN IN MILK

Health implications of milk containing beta-casein with the A2 genetic variant
Bell SJ, Grochoski GT, Clarke AJ. (2006). Crit RevFood Sci Nutr 46(1):93-100.

Polymorphism of bovine beta-casein and its potential effect on human health
Kaminski S, Cieslinska A, Kostroyra E. (2007) J Appl Genet. 48(3):189-98.

The A2 milk case: a critical review
Truswell AS. (2005) Eur J Cln Nutr. 59(5):623-31

A critique of Truswell's A2 milk review
Woodford KB. (2006) Eur J Clin Nutr. 60(3):437-9

Further research for consideration in 'the A2 milk case'
Allison AJ, Clark AJ. (2006) EurJ Clin Nutr.60(7):921-4;924-5. Epub 2005 Sep 28

A2 Milk, Farmer Decisions, and Risk Management
Woodford K (2007) Proceedings of the 16th International Farm Management Association Congress, Peer Reviewed Papers Vol2, pp 641-648. University College, Cork,(Eds S. O'Reilly, M. Keane, P. Enright. ISBN:978-92-990038-3-1).

Scientific Report of EFSA prepared by a DATEX Working Group on the potential health impact of β-casomorphins and related peptides
EFSA Scientific Report (2009) 231, 1-107

CHILDHOOD (TYPE 1) DIABETES

Epidemiological (Population) Studies

Lower consumption of cow milk protein A1 beta-casein at 2 years of age, rather than consumption among 11- to 14-year-old adolescents, may explain the lower rate of type 1 diabetes in Iceland than in Scandinavia.
Birgisdottir BE, Hill JP, Thorsson AV, Thorsdottir I. (2006) Ann Nutr Metab. 50(3):177-83.

Variation in consumption of cow milk proteins and lower rate of Type 1 diabetes in Iceland versus the other 4 Nordic countries..
Birgisdottir BE, Hill JP, Harris DP, Thorsdottir I. 2002. Diabetes Nutr. Metab. 15 (4) 240-245

Ischaemic heart disease, Type 1 diabetes, and cow milk A1 beta-casein
Laugesen M & Elliott R, 2003. New Zealand Medical Journal 116(1168) U295.

Different beta-casein fractions in Icelandic versus Scandinavian cow's milk may influence diabetogenicity of cow's milk in infancy and explain low rate of insulin-dependent diabetes mellitus in Iceland.
Thorsdottir I, Birgisdottir BE, Johannsdottir IM, Harris DP, Hill J, Steingrimsdottir L, Thorsson A (2000) Pediatrics 106(4):719-24.

b-casein A1 consumption and incidence of Type 1 Diabetes in Germany.
Wasmuth, H.E., Rosenbauer, J., Elliott, RB., Mclachlan, C., Erhardt, G., Giani, G., Kolb, H.: Kongress der Europäischen Diabetesgesellschaft vom 28.-30.09.1999 in Brüssel/Belgien (Conference Presentation)

Type 1 (insulin-dependent) diabetes mellitus and cow milk: casein variant consumption.
Elliott RB, Harris DP, Hill JP, Bibby NJ, Wasmuth HE. 1999.. Diabetologia 42 (3)292-296.

Human Studies

[The significance of A1 and A2 antibodies against beta-casein in type-1 diabetes mellitus].
Padberg S, Schumm-Draeger PM, Petzoldt R, Becker F, Federlin K. 1999. (Article in German.) Dtsch Med Wochenschr. 124 (50) 1518-21.

Antibodies to bovine beta-casein in diabetes and other autoimmune diseases.
Monetini L, Cavallo MG, Manfrini S, Stefanini L, Picarelli A, Di Tola M, Petrone A, Bianchi M, La Presa M, Di Giulio C, Baroni MG, Thorpe R, Walker BK, Pozzilli P (2002). Horm Metab Res. 34 (8) 455-9.

Bovine beta-casein antibodies in breast- and bottle-fed infants: their relevance in Type 1 diabetes.
Monetini L, Cavallo MG, Stefanini L, Ferrazzoli F, Bizzarri C, Marietti G, Curro V, Cervoni M, Pozzilli (2001) P. Diabetes Metab Res Rev. 17(1):51-4

Beta-casein in cow's milk: A major antigenic determinant for type 1 diabetes?
Pozzilli P. 1999. Journal of Endocrinological Investigations 22 (7) 562-567

Immunosuppressing effects of cow milk beta casomorphin in prediabetic mice and humans
R.B. Elliott, H. Wasmuth and J. Hill. (1997) 16th IDF Congress, Helsinki.

Animal Studies and Mechanistic Support

The role of ß-casein variants in the induction of insulin-dependent diabetes in the non-obese diabetic mouse and humans.
Elliott RB, Wasmuth HE, Bibby NJ, Hill JP: Seminar on milk protein polymorphism, IDF special issue no. 9702. International Dairy Federation, Brussels, 445–453, 1997

The effects of Casomorphin-7 on NOD mouse macrophage oxidation and primary immune response
American Diabetes Association 58th Annual Meeting and Scientific Session, Chicago 1998

Influence of b-casomorphins on the function of the endocrine pancreas: ß-Casomorphins and Related Peptides: Recent Developments.
Zuhlke H. Damert A. Eckhardt W. Hubner G. Kauschke R. Salazar R. Neubert K. (Brantl V. and Teschemacher H., eds.) VCH, Weinheim, 1994,, p161-

HEART DISEASE AND CARDIOVASCULAR DISEASE

Epidemiological (Population) Studies

beta-casein A1, ischaemic heart disease mortality, and other illnesses.
McLachlan, C. N. S. 2001. Medical Hypotheses. 56(2): 262-272

Ischaemic heart disease, Type 1 diabetes, and cow milk A1 beta-casein.
Laugesen M & Elliott R, 2003. New Zealand Medical Journal 116(1168) U295.

Human Studies

Significant increase in antibodies against oxidized LDL particles (Igox LDL) in three-month old infants who received milk formula.
Steinerová A, Racek J, Rajdl D, Stoicky F, Rokyta Z, Trefil L, Korotvik a M 2004 Letter to the Editor. 173(1) pp 147-148

Autoantibodies against oxidised LDL in the first phase of life. Low density lipoproteins.
Steinerova A, Racek J, Stozicky F, Tatzber F, Lain A 1999.. Clin. Chem. Lab. Med. 37(9), pp 913-7

Antibodies against oxidised LDL in infants.
Steinerova A, Racek J, Stozicky F, Tatzber F, Zima T, Setina R. 2001. Clin. Chem. 47(6) pp 1137-8

Effect of dietary supplementation with beta-casein A1 or A2 on markers of disease development in individuals at high risk of cardiovascular disease.
Chin-Dusting J, Shennan J, Jones E, Williams C, Kingwell B, Dart A. (2006) Br J Nutr. 95(1):136-44

A comparison of the effects of A1 and A2 beta-casein protein variants on blood cholesterol concentrations in New Zealand adults.
Venn BJ, Skeaff CM, Brown R, Mann JI, Green TJ. (2006). Atherosclerosis. 188(1):175-8. Epub 2005 Nov 18.

Animal Studies and Mechanistic Support

A casein variant in cow's milk is atherogenic.
Tailford KA, Berry CL, Thomas AC, Campbell JH. 2003 Atherosclerosis. 170(1):13-9.

Casein-derived peptides can promote human LDL (low-density lipoproteins) oxidation by a peroxidase-dependent & metal-independent process.
Torreilles J & Guerin MC. 1995. C R Seances Soc Biol Fil 189(5):933-42

Antihypertensive effect of the peptides derived from casein by an extracellular proteinase from Lactobacillus helveticus CP790.
o Yamamoto N, Akino A, Takano T. J Dairy Sci. 1994 Apr;77(4)917-22

BETA-CASEIN PEPTIDES LINKED TO SYMPTOMS OF NEUROLOGICAL CONDITIONS

Human Studies

Milk containing beta-casein with proline at position 67 does not aggravate neurological disorders.
Crawford RA, Boland MJ, Norris CS, Hill JP, Fenwick RM. 2002, PCT WO0219832.

Autism and urinary exogenous neuropeptides: development of an online SPE–HPLC–tandem mass spectrometry method to test the opioid excess theory.
Dettmer K, Hanna D, Whetstone P, Hansen R, Hammock BD. 2007. Analytical and Bioanalytical Chemistry. (Advance online publication May 2007. DOI 10.1007/s00216-007-1301-4).

Can the pathophysiology of autism be explained by the nature of the discovered urine peptides?
Reichelt KL, Knivsberg AM. (2003) Nutritional Neuroscience 6(1):19-28.

Autism and Schizophrenia: Intestinal Disorders.
Cade R et al. (2000) Nutritional Neuroscience 3: 57-72.

Reports on dietary intervention in autistic disorders.
Knivsber AM, Reichelt KL, Nodland M. (2001). Nutritional Neuroscience. 4(1):25-37

A randomised, controlled study of dietary intervention in autistic syndromes.
Knivsberg AM, Reichelt KL, Høien T, Nødland M. (2002). Nutritional Neuroscience 5(4):251-61hin-Dusting J, Shennan J, Jones E, Williams C, Kingwell B, Dart A. (2006) Br J Nutr. 95(1):136-44

The gluten-free, casein-free diet in autism: results of a preliminary double blind clinical trial.
Elder JH, Shankar M, Shuster J, Theriaque D, Burns S, Sherrill L. 2006. Journal of Autism and Developmental Disorders 36(3):413 420.

Elimination diets in autism spectrum disorders: any wheat amongst the chaff?
Christison GW, Ivany K. 2006. Journal of Developmental & Behavioral Pediatrics. 27(2Suppl):S162–171.

Animal Studies and Mechanistic Support

Rotational behaviour produced by intranigral injections of bovine and human beta-casomorphins in rats.
Herrera-Marschitz M, Terenius L, Grehn L, Ungerstedt U.. 1989. Psychopharmacology (Berl).99(3):357-61

ß-Casomorphin Induces Fos-Like Immunoreactivity in Discrete Brain Regions Relevant to Schizophrenia and Autism.
Zhongjie Sun, J. Robert Cade, Melvin J. Fregly, R. Malcolm Privette. University of Florida, USA. Autism, Vol. 3, No. 1, 67-83 (1999).

In vitro penetration of des-tyrosine1-D-phenylalanine3-beta-casomorphin across the blood-brain barrier.
Stark H, Van Bree JB, de Boer AG, Jaehde U, Breimer DD. (1992) Peptides. 13(1):47-51.

Saturable transport of peptides across the blood-brain barrier.
Banks WA, Kastin AJ. (1987) Life Sci. 41(11):1319-38.

BIOACTIVE DIGESTION PRODUCTS OF BETA-CASEIN VARIANTS

Enzymatic release of neocasomorphin and beta-casomorphin from bovine beta-casein.
Jinsmaa, Y & Yoshikawa, M. (1999). Peptides V20(8), pp 957-962.

Multifunctional peptides encrypted in milk proteins.
Meisel H. (2004). Biofactors 21(1-4):55-61.

Effects of Milk-derived bioactives: an overview.
Shah, N. (2000). British Journal of Nutrition. 84. Suppl. 1. S3-310.

Biologically active peptides in milk proteins.
Meisel H, Frister H, Schlimme E. Z Ernahrungswiss. (1989) Dec;28(4)267-78

Purification and identification of potentially bioactive peptides from enzyme-modified cheese.
Haileselassie SS, Lee BH, Gibbs BF. J Dairy Sci. 1999 Aug;82(8):1612-7.

Database of biologically active peptide sequences.
Dziuba J, Minkiewicz P, Nalecz D, Iwaniak A. Nahrung. 1999 Jun;43(3):190-5. Review.

Identification of Peptides Derived from B-casein Hydrolysates by Proteolytic Enzymes.
Park, S. Y. Gibbs B. F. Lee B. H. 1996. Korean J. Dairy Sci. 18 (4):237-246. (Korean)

BETA-CASOMPORPHINS (BCMs) – PRODUCTION AND ABSORPTION

Enzymatic release of neocasomorphin and beta-casomorphin from bovine beta-casein.
Jinsmaa, Y & Yoshikawa, M. (1999). Peptides V20(8), pp 957-962.

Demonstration of beta-casomorphin immunoreactive materials in in vitro digests of bovine milk and in small intestine contents after bovine milk ingestion in adult humans.
Svedberg J, de Haas J, Leimenstoll G, Paul F, Teschemacher H. Peptides. 1985 Sep-Oct;6(5):825-30.

Casein peptide release and passage to the blood in humans during digestion of milk or yogurt
Chabance B, Marteau P, Rambaud JC, Migliore-Samour D, Boynard M, Perrotin P, Guillot R, Jolles P, Fiat AM 1998.. Biochimie 80(2), pp 155-165.

beta-Casomorphin-immunoreactivity in the brain stem of the human infant.
Pasi A, Mahler H, Lansel N, Bernasconi C, Messiha FS.1993 Res Commun Chem Pathol Pharmacol. 80(3):305-22.

Demonstration of a beta-casomorphin immunoreactive material in the plasma of newborn calves after milk intake.
Umbach M, Teschemacher H, Praetorius K, Hirschhauser R, Bostedt H. 1985. Regul Pept. Nov 7;12(3):223- 30. • Link:

ß-Casomorphin Induces Fos-Like Immunoreactivity in Discrete Brain Regions Relevant to Schizophrenia and Autism.
Zhongjie Sun, J. Robert Cade, Melvin J. Fregly, R. Malcolm Privette. University of Florida, USA. Autism, Vol. 3, No. 1, 67-83 (1999).

In vitro penetration of des-tyrosine1-D-phenylalanine3-beta-casomorphin across the blood-brain barrier.
Stark H, Van Bree JB, de Boer AG, Jaehde U, Breimer DD. (1992) Peptides. 13(1):47-51.

Saturable transport of peptides across the blood-brain barrier.
Banks WA, Kastin AJ. (1987) Life Sci. 41(11):1319-38.

BETA-CASOMORPHINS – BIOLOGICAL ACTIVITY OF BCM-7

Gastrointestinal Effects

Inhibition of small intestine motility by casein: a role of beta casomorphins?
Defilippi C, Gomez E, Charlin V, Silva C. 1995. Nutrition 119(6):751–754.

Effects of beta-casomorphin derivatives on gastrointestinal transit in mice.
Becker A, Hempel G, Greksch G, Matthies H. (1990) Biomedica Biochimica Acta 49(110):1203–1207.

Beta-casomorphin-7 regulates the secretion and expression of gastrointestinal mucins through a mu-opioid pathway.
Zoghbi S, Trompette A, Claustre J, El Homsi M, Garzon J, Jourdain G, Scoazec J,Plaisancie P. 2006. American Journal of Physiology.Gastrointestinal and Liver Physiology 290:G1105–G1113.

Milk bioactive peptides and beta-casomorphins induce mucus release in rat jejunum
Trompette A, Claustre J, Caillon F, Jourdan G, Chayvialle JA, Plaisancié P. (2003) J Nutr. Nov;133(11):3499-503.

Effects of peptides derived from dietary proteins on mucus secretion in rat jejunum.
Claustre J, Toumi F, Trompette A, Jourdan G, Guignard H, Chayvialle JA, Plaisancié P. (2002) Am J Physiol Gastrointest Liver Physiol. 3(3):G521-8.

Treatment of acute secretory diarrhea with casein: an effect of beta-casomorphins?][Article in Spanish]
Charlin V, Defilippi C, Vargas V, Borghesi L, Gómez E. (1992) Rev Med Chil. 20(6):666-9.

Effects on Immune Cell and Functions

Pseudoallergic skin reactions to opiate sequences of bovine casein in healthy children
Kurek M, Czerwionka-Szaflarska M, Doroszewska G. 1995.. Rocz Akad Med Bialymst. 40(3):480-5.

A naturally occurring opioid peptide from cow's milk, beta casomorphine-7, is a direct histamine releaser in man.
Kurek M, Przybilla B, Hermann K, Ring J. 1992.. Int Arch Allergy Immunol. 97(2):115-20.

The effects of Casomorphine-7 on NOD mouse macrophage oxidation and primary immune response
American Diabetes Association 58th Annual Meeting and Scientific Session, Chicago 1998

Stimulation of human peripheral blood lymphocytes by bioactive peptides derived from bovine milk proteins.
Kayser H, Meisel H. FEBS Lett. 1996 Mar 25;383(1-2):18-20.

Respiratory Effects

Relation of beta-casomorphin to Apnea in Sudden Infant Death Syndrome
Sun Z, Zhang Z, Wang X, Cade R, Elmir Z, Fregly M. 2003.. Peptides 24(6):937-943.

beta-Casomorphins induce apnea and irregular breathing in adult rats and newborn rabbits.
Hedner J, Hedner T. 1987 Life Sci 41(20):2303-12.

Effect of beta-casomorphin on neonatal sleep in rats.
Taira T, Hilakivi LA, Aalto J, Hilakivi I. 1990. Peptides 11(1):1–4.

Behavioral & Endocrinological Effects

Rotational behaviour produced by intranigral injections of bovine and human beta-casomorphins in rats.
Herrera-Marschitz M, Terenius L, Grehn L, Ungerstedt U.. 1989. Psychopharmacology (Berl).99(3):357-61

Delayed behavioral effects of beta-casomorphin-7 depend on age and gender of albino rat pups.
Dubynin VA, Malinovskaya IV, Ivleva YA, Andreeva LA, Kamenskii AA, Ashmarin, IP 2000. . Bull. Exp. Biol. Med. 130(11), pp1031-1034.

Casein, a prohormone with an immunomodulating role for the newborn?
Migliore-Samour D, Jolles P. Experientia. 1988 Mar 15;44(3):188-93. Review.

Casomorphins reduce separation distress in chicks.
Panksepp J, Normansell L, Siviy S, Rossi J 3rd, Zolovick AJ.1984 Peptides 5(4):829-31

Effects of intra-abomasal infusion of beta-casomorphins on circulating concentrations of hyperglycaemic insulin and glucose in dairy cows.
Kim TG, Choung JJ, Wallace RJ, Chamberlain DG. 1: Comp Biochem Physiol A Mol Integr Physiol. 2000 Nov;127(3):249-57.

Effect of beta-casomorphins on somatostatin release in dogs.
Schusdziarra V, Schick R, de la Fuente A, Holland A, Brantl V, Pfeiffer EF. (1983) Endocrinology. Jun;112(6):1948-51.

Effect of beta-casomorphins and analogs on insulin release in dogs.
Schusdziarra V, Schick A, de la Fuente A, Specht J, Klier M, Brantl V, Pfeiffer EF. 1: Endocrinology. 1983 Mar;112(3):885-9.

Beta-Casein Variant Genetics

Milk protein polymorphism: detection and diffusion of the genetic variants in Bos genus.
P. Formaggioni, A. Summer, M. Malacarne, P. (1999). Mariani Università degli Studi di Parma, Annali della Facoltà di Medicina Veterinaria Vol. XIX

Genetic Polymorphism of Milk Proteins (Chapter 16).
Ng-Kwai-Hang, K.F., and F. Grosclaude. (2002). Chapter 16 pp 737-814 In Advanced Dairy Chemistry: Volume 1 – Proteins, 2nd Edition (edited by P.F. Fox and P. L. H. McSweeney). Kluwer Academic/Plenum Publishers, New York

Association between milk protein genetic variants and genetic values of Canadian Holstein bulls for milk yield traits.
Sabour MP, Lin CY, Lee AJ, McAllister AJ..J Dairy Sci. 1996 Jun;79(6):1050-6.

Casein polymorphism and relation between milk production traits.
G. Freyer, Z. Liu, G. Erhardt, L. Panicke. (1999). Journal of Animal Breeding and Genetics 116 (2), 87–97.

Milk Protein Polymorphisms in California Dairy Cattle.
Alison van Eenennaam and Juan Fernando Medrano. (1991). J Dairy Sci 74:1730-1742

Associations between β-casein genotype and milk yield and composition in grazing dairy cows
Morris CA, Hickey SM, Cullen NG, Prosser CG, Anderson RM, Tate ML. 2005. New Zealand Journal of Agricultural Research 48:441–450.

Milk protein loci polymorphism in taurine (Bos taurus) and zebu (Bos indicus) populations bred in hot climate.
G. Ceriotti, D. Marletta, A. Caroli, G. Erhardt. (2004). Journal of Animal Breeding and Genetics 121 (6), 404– 415.