



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : C12N 15/12, C07K 14/47, C12Q 1/68, C12N 5/10, 5/16, C07K 16/18, G01N 33/53, A61K 38/17, 7/00	A2	(11) International Publication Number: WO 96/05309 (43) International Publication Date: 22 February 1996 (22.02.96)
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(21) International Application Number: PCT/US95/10479

(22) International Filing Date: 17 August 1995 (17.08.95)

(30) Priority Data:

08/292,345	17 August 1994 (17.08.94)	US
08/347,563	30 November 1994 (30.11.94)	US
08/438,431	10 May 1995 (10.05.95)	US
08/483,211	7 June 1995 (07.06.95)	US

(60) Parent Application or Grant

(63) Related by Continuation

US	08/483,211 (CIP)
Filed on	7 June 1995 (07.06.95)

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(81) Designated States: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, US, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, MW, SD, SZ, UG).

Published

Without international search report and to be republished upon receipt of that report.

(54) Title: MODULATORS OF BODY WEIGHT, CORRESPONDING NUCLEIC ACIDS AND PROTEINS, AND DIAGNOSTIC AND THERAPEUTIC USES THEREOF

(57) Abstract

The present invention relates generally to the control of body weight of animals including mammals and humans, and more particularly to materials identified herein as modulators of weight, and to the diagnostic and therapeutic uses to which such modulators may be put. In its broadest aspect, the present invention relates to the elucidation and discovery of nucleotide sequences, and proteins putatively expressed by such nucleotides or degenerate variations thereof, that demonstrate the ability to participate in the control of mammalian body weight. The nucleotide sequences in object represent



the genes corresponding to the murine and human OB gene, that have been postulated to play a critical role in the regulation of body weight and adiposity. Preliminary data, presented herein, suggests that the polypeptide product of the gene in question functions as a hormone. The present invention further provides nucleic acid molecules for use as molecular probes, or as primers for polymerase chain reaction (PCR) amplification, i.e., synthetic or natural oligonucleotides. In further aspects, the present invention provides a cloning vector, which comprises the nucleic acids of the invention; and a bacterial, insect, or a mammalian expression vector, which comprises the nucleic acid molecules of the invention, operatively associated with an expression control sequence. Accordingly, the invention further relates to a bacterial or a mammalian cell transfected or transformed with an appropriate expression vector, and correspondingly, to the use of the above-mentioned constructs in the preparation of the modulators of the invention. Also provided are antibodies to the OB polypeptide. Moreover, a method for modulating body weight of a mammal is provided. In specific examples, genes encoding two isoforms of both the murine and human OB polypeptides are provided.