BRIEF REPORTS

Mapping of the Gene Encoding the Melanocortin-1 (α-Melanocyte Stimulating Hormone) Receptor (MC1R) to Human Chromosome 16q24.3 by Fluorescence *in Situ* Hybridization

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α-Melanocyte stimulating hormone (α-MSH), a hormone originally named for its ability to regulate pigmentation of melanocytes, is a 13-amino-acid post-translational product of the pro-opiomelanocortin (POMC) gene. α MSH and the other products of POMC processing, which share the core heptapeptide amino acid sequence Met-Glu (Gly) His-Phe-Arg-Trp Gly (Asp), the adrenocorticotropic hormone (ACTH), β-MSH, and γ-MSH, are collectively referred to as melanocortins. While best known for their effects on the melanocyte (pigmentation) and adrenal cortical cells (steroidogenesis), melanocortins have been postulated to function in diverse activities, including enhancement of learning and memory, control of the cardiovascular system, analgesia, thermoregulation, immunomodulation, parturition, and neurotrophism (1–7).

Recent studies have described an unexpected diversity of subtypes of receptors for the melanocortin peptides and determined that they all belong to the superfamily of seven transmembrane G-protein-linked cell surface receptors (8–11). The α-MSH receptor is identified as the melanocortin-1 receptor, the adrenocorticotropic hormone (ACTH) receptor as the melanocortin-2 receptor, a third receptor that is present in the brain and placenta as the melanocortin-3 receptor, and a fourth receptor that is present primarily in the brain as the melanocortin-4 receptor. Using the technique of fluorescence *in situ* hybridization (FISH), we have previously reported the mapping of the genes for the human melanocortin-2, -3, and -4 receptors to human chromosomes 18p11.2, 20q13.2–q13.3, and 18q21.3, respectively (11, 12). As in the case of most other seven-transmembrane G-protein-linked receptor subfamilies, the melanocortin receptors are not clustered at a single locus.

To identify the chromosomal band encoding the human melanocortin-1 receptor (MC1R)[2] gene, 1 μg of an EMBL clone (MC1R; obtainable from I.G. upon request) containing the coding region of the human MC1R and approximately 15 kb of surrounding DNA (10) was labeled with biotin and hybridized to human metaphase chromosomes as previously described (13). A total of 24 metaphase cells were examined, and all cells examined had "double" fluorescent signals localized to the terminal long arm of chromosome 16 (Figs. 1A and 1B). In all 24 cells examined, double signals were observed on both chromosome 16 homologs. In all cases, the identical cells hybridized for FISH previously had been G-banded (using trypsin–

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[2] MC1R is the gene symbol designated by the Human Gene Mapping Nomenclature Committee.

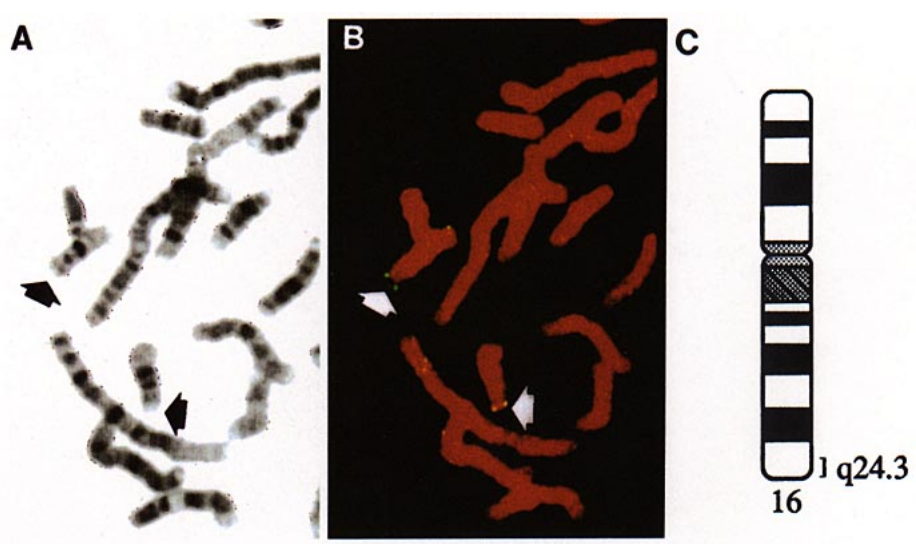

FIG. 1. Localization by FISH of the gene encoding the melanocortin-1 (α-MSH) receptor to 16q24.3. (**A**) G-banded partial metaphase chromosomes (arrows indicate chromosomes 16). (**B**) Partial metaphase identical to **A** after FISH with the biotin-labeled melanocortin-1 receptor probe documenting localization to distal 16q. (**C**) Idiogram of chromosome 16.

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Giemsa) and photographed to allow direct comparison of FISH and banding results. The results indicate that the human MC1R gene is localized to 16q24.3 (Fig. 1C).

This localization is of particular interest in view of the finding that the comparative region of mouse chromosome 8 has previously been described to be the site of the extension locus that controls mammalian coat color (14). Robbins *et al.* (15) have shown that extension locus alleles are a result of four naturally occurring point mutations in the mouse α-MSH receptor. The resultant functional differences between the various α-MSH receptor genotypes at this locus lead to different phenotypic characteristics. Whether similar mutations occur in man to account for variation in hair coloration remains to be determined.

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