Cas d'étude: la maladie d'Alzheimer

Figure 1: hippocampe (en rouge).

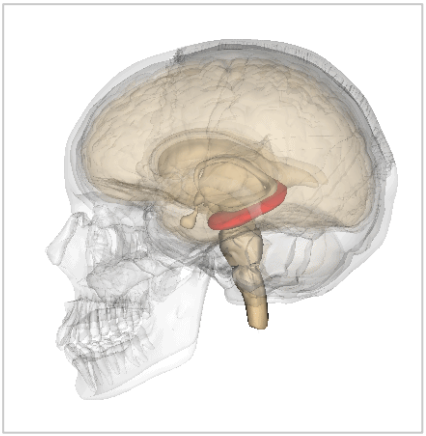

Figure 2: le peptide beta-amyloïde. Gauche: Le précurseur traverse la membrane du neurone. Il peut être clivé (coupé) à différents endroits par des enzymes spécifiques (secrétases). Droite: Structure 3D du peptide résultant du clivage.

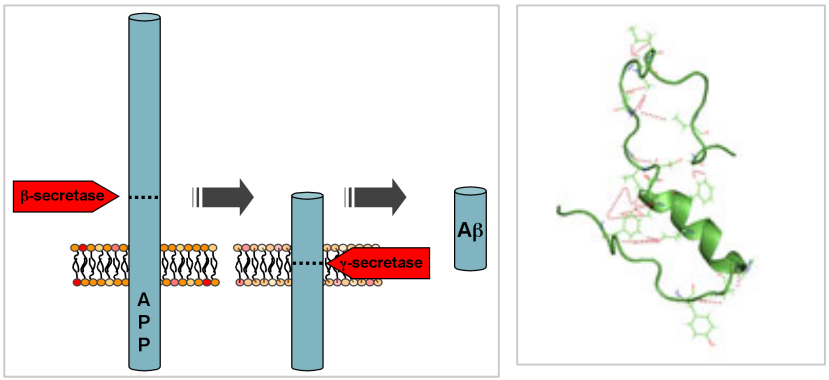

Figure 3: étude de liaison génétique. La partie du haut montre le pédigrée d'une famille où se transmet l'Alzheimer. Les patients sont marqués en noir. La partie du bas schématise l'origine (paternelle, maternelle) du chromosome 21. Les chromosomes noirs et blancs proviennent d'événements de recombinaisons. *Source: Goate et al. (1991) Segregation of a missense mutation in the amyloid precursor protein gene with familial Alzheimer's disease. Nature, **349**, 704–706.*

FIG. 1 Pedigree in which early-onset AD is apparently inherited as an autosomal dominant disorder. The average age of onset in this family is 57 ± 5 yr. Black symbols denote affected individuals and oblique lines indicate individuals who are deceased. Females are denoted by circles and males by squares. Triangles are used in the present generation to preserve anonymity. In generation II the spouses of the two affected brothers were sisters. Samples were available from the 13 individuals whose haplotypes are illustrated, from a further 19 children and spouses of these individuals and from 7 more distantly related unaffected individuals. Beneath the pedigree are ideograms of the two chromosomes 21 in each individual of the third generation at four loci on the long arm of the chromosome. The linkage data suggest that the chromosomes filled in in black were inherited from the affected fathers.

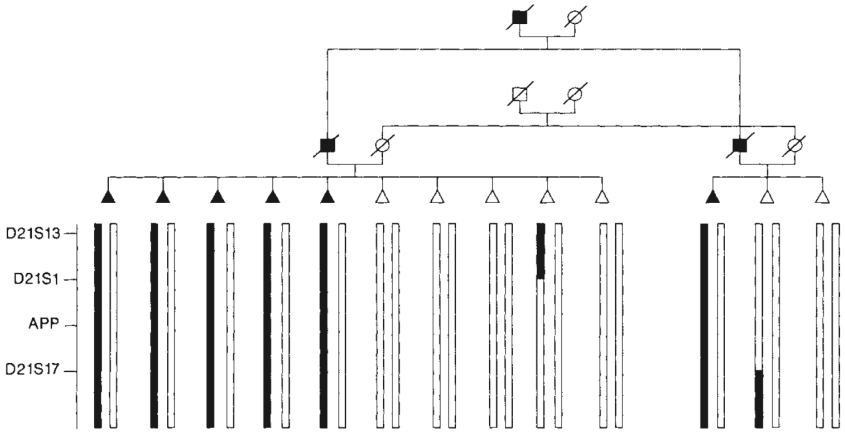

Figure 4: étude d'association à échelle génomique. L'axe horizontal correspond la position génomique, où chaque chromosome est indiqué par une couleur spécifique. Chaque point correspond à un marqueur de type "*single-nucleotide polymorphism*" (SNP). La position verticale indique la significativité de l'association entre un SNP et la fréquence de la maladie.

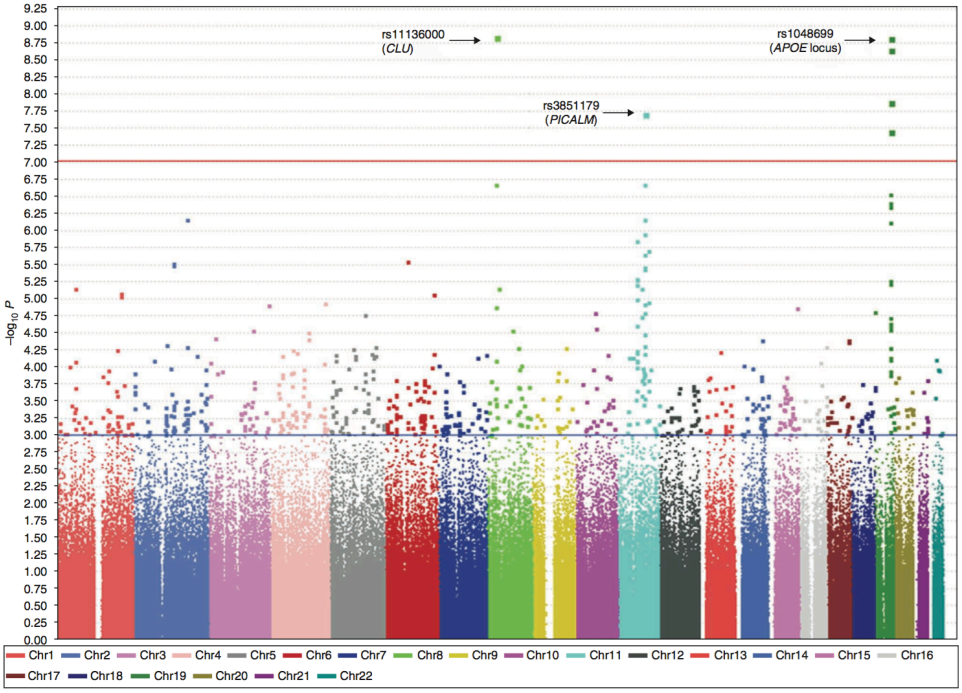

Figure 1 Scatterplot of chromosomal position (*x* axis) against $-\log_{10}$ GWAS *P* value (*y* axis). The *y*-axis scale has been limited to 9.25 ($P = 5.6 \times 10^{-10}$), although highly significant association was observed with SNPs in the vicinity of the *APOE* locus (for example, rs2075650 with $P = 1.8 \times 10^{-157}$). The threshold for genome-wide significance ($P \leq 9.4 \times 10^{-8}$) is indicated by the red horizontal line. 761 SNPs with $P \leq 1 \times 10^{-3}$ lie above the blue horizontal line and are listed in **Supplementary Table 2**. The plot was produced using Haploview version 4.0 (ref 49.).

Source: Harold,D., *et al.* (2009) Genome-wide association study identifies variants at CLU and PICALM associated with Alzheimer's disease. *Nat Genet*, **41**, 1088–1093.