of chromosome 1q, suggesting that it was added independently of HSPRY3. None of the PAR2 genes mapped to the same regions of the marsupial genome as PAR1 genes, implying that PAR1 and PAR2 evolved by independent additions to an ancestral mammalian proto-X/Y.

#310

The Complete Genome Sequence of the Human ADH Gene Family

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Human Alcohol Dehydrogenase (ADH) gene family, which includes seven members, locates in chromosome 4q22-23 region. This family encodes five classes of cytosolic isozymes based upon structural and functional distinctions, and these proteins catalyze the reversible oxidation of a wide variety of xenobiotic and endogenous alcohols to corresponding aldehydes. In addition, ADH1 and ADH4 also act as retinal dehydrogenase and may be related to ethanol toxicity. To understand the structure, regulation, and functions of these ADHs, BAC clones from the 4q22-23 region were selected, sequenced, and assembled. A contig consisting of three BAC clones covered all ADH loci, and the entire ADH complex spans over 490 kb. All seven ADH genes have the same orientation and they are separated into two clusters. The ADH1, ADH2, ADH3 and ADH7 are within a region of about 170 kb, while a second cluster contains ADH5, ADH4 and ADH6 and occupies about 150 kb. On the basis of genomic sequences, the structure of each ADH gene and the non-coding intergenic regions can be addressed. The evolutionary significance and applications of the complete human ADH genome sequence will be present in the meeting.

#311

The Sequences Map of Human Chromosome 20

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The effort to produce one third of the human genome's draft sequence at teh Sanger Centre by the spring of the year 2000 is well under way. In parallel, however, we actively pursue our ultimate goal of producing the finished and annotated sequence.

Mapping and sequencing chromosome 20 is a project that started almost from scratch some 3 years ago at the Sanger Centre. We are constructing a sequence-ready bacterial clone, map which currently covers over 83% of the chromosome and it is in 16 contigs. Contigs are assembled by fingerprinting and STS content analysis. We have used 2,261 STSs and identified / analysed a total of 9,324 positive clones (6,395 PACs adn 2,929 BACs). Of those STSs, 834 are derived from end-sequences of clones. Sizing of the remaining gaps is underway by interphase and fibre FISH analysis. Preliminary data suggest that coverage could be significantly higher than 83% especially if we account for centromeric and telomeric repeat regions.

Our sequencing strategy remains "deep" shotgun sequencing in the form of a semi-automated process. Thus far a non-redundant set of 533-clones have entered the sequencing pipeline with a current output of 33.37 Mb unfinished and 23.02 Mb finished sequence, respectively (as per 31.12/99). Beside extensive redundancy in the figure of unfinished sequence data, we estmate that the combined sequence output represents over 55% of the total. Computational sequence analysis of 13.49 Mb of finished data has identified 55 known human genes, 66 putative novel genes, and 35 pseudogenes. Of the putative novel genes, 21 have so far been confirmed experimentally.

It is part of our policy to co-ordinate our mapping and sequencing efforts with teh rst of the community. Our mapping and sequence analysis data are stored in an implementation of the database ACEDB, known as 20ace, which is available at ftp://ftp.sanger.acuk/pub/human/chr20/. In addition a weekly released version of 20ace can be accessed via a WWW browser using Webace. All the links to data including progress on the sequencing status of a given clone, can be found at http://www.sanger.ac.uk/HGP/Chr20.

#312

Analysis and annotation of 5 Mb of draft and finished sequence from 16q12

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We have completed a map and chosen a tiling set of ~ 45 spanning BACs, most often from the RPCI-11 library, for a region that covers more than 5 Mb of human 16q12, encompassing a locus for inflammatory bowel disease (IBD1). These BACs have been selected by a combination of overgo hybridization, restriction map assembly by both fingerprinting and sequence prediction, and BAC end sequence searches. Sequencing has been completed to levels ranging from light shotgun to Bermuda finished bases. We will present annotation and statistical results of our analysis of the sequence we have obtained thus far and show how these results compare with ~ 5 Mb of sequence from 16p13.3. Supported by the US DOE, OBER under contract W-7405-ENG-36.

#313

Assignment of a psoriasis susceptibility locus on chromosome 2q35 found by a genome-wide scan in a large Danish family.

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Psoriasis is a common chromic skin disease, affecting about 2% of the Caucasian population (McKusick = 177900, 1992). It is characterized by epidermal hyperplasia, extremely rapid proliferation and altered differentiation of keratinocytes, an abnormal collection of polymorphonuclear leucocytes in the epidermis, and a mononuclear cell infiltrate in the underlying dermis. A large pedigree has been collected for studying more than 500 DNA markers for mapping the disease. In this single extended famil, which comprises 20 persons, a maximum lod score of z=3.98 to D2S128 in the chromosome area 2q35 was obtained. A penetrance of 0.65 and a phenocopy of 0.05 were used for calculation of the lod score. An other skin disease region. The gene for this disease could also be a candidate gene for psoriasis in the present family. We could not confirm the previously reported indications of linkage to the common locus on chromosomes 1cen, 3q21, 4p, 6p, 16q, 17q and 20 in this family and other families in our material.

#314

Sib similarity in Danish Families

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Penrose introduced sib-pair analysis in 1935: an essential feature was that ascertainment was not biased by selection for sibships with more than one affected sib. (www.gene.ucl.ac.uk/anhumgen/). Most recent sib-pair studies are restricted to affected sib pairs and analysed on the assumption that the parental gametes deduced from genotypes are representative of those present before fertilisation with each allele having an equal chance of both achieving fertilisation and surviving birth.

Such equality is not to be expected in view of the losses between conception and birth. It is likely that these are due mainly to embryonic lethals usually leading to excess similarity of alleles from nearby loci . There are few data relating to sib-similarity in normal sibs, the 'controls', necessary for any secure inference based on any single set of data on affected sib-pairs. The extensive data from the CEPH families are well known: a subset typed at Marshfield is