(from position 153 to 166; Fig. 1). Colinearity of two independent cDNAs over the high and low conservation domains excludes the possibility of chimeric clones. The low conservation domain contains a proline-rich segment (17% prolines from position 181 to 292), which is significantly shorter than the human proline-rich region and is not predicted to contain a PEST segment (Pro+Glu+Ser+Thr-rich segment; [4]), unlike the human one. The X11 encoded protein seems, therefore, formed of two moieties. The N terminal moiety is variable through evolution, while the C terminal moiety is highly conserved and contains a putative transmembrane segment, pinpointing to potentially functionally important domains in this portion of the protein.

References:
1. Duclos, F., Buschert, V., Sirugo, G., Mandel, J.-L., Hen, R., Koenig, M. (1993). Proc. Natl. Acad. Sci. USA 90, 109–113.
2. Rodius, F., Duclos, F., Wrogemann, K., LePaslier, D., Ougen, P., Billault, A., Belal, S., Musenger, C., Brice, A., Dürr, A., Mignard, C., Sirugo, G., Weissenbach, J., Cohen, D., Hentati, F., Hamida, M.B., Mandel, J.-L., Koenig, M., (1994). Am. J. Hum. Genet. 54, 1050–1059.
3. Duclos, F., Rodius, F., Wrogemannk, K., Mandel, J.-L., Koenig, M., (1994). Hum. Mol. Genet. 3, 909–914.
4. Rogers, S., Wells, R., Rechsteiner, M., (1986). Science 234, 364–368.

Chromosomal localization of the large subunit of mouse replication factor C in the mouse and human

A.C. Lossie,[1] B.R. Haugen,[2] W.M. Wood,[2] S.A. Camper,[1] D.F. Gordon[2]

[1]Department of Human Genetics, The University of Michigan Medical School, Ann Arbor, Michigan 48109–0618, USA
[2]Department of Medicine, University of Colorado Health Science Center, Denver, Colorado 80262, USA

Received: 1 July 1994 / Accepted: 13 September 1994

Species: Mouse and human
Locus name: 140 kDa subunit of DNA replication factor C complex. This 5-subunit complex is a DNA-activated ATPase that complexes with proliferating cell nuclear antigen and DNA polymerase δ to direct the synthesis of both the leading and lagging strands at the replication fork [1].
Locus symbol: *Recc1,* RECC1
Map position: *Recc1* is localized on mouse Chr 5: centromere–*D5Mit1*–4.3 ± 2.1–*Xmv45*–6.4 ± 2.5–*Mpmv7*–8.6 ± 2.9–*D5Bir9*–2.7 ± 1.9–*Recc1*–5.4 ± 2.6–*Pmv11*–1.1 ± 1.1–*D5Bir1*–telomere. RECC1 is assigned to human Chr 4.
Method of mapping: *Recc1* was localized by haplotype analysis of 71 progeny from an interspecific backcross, (C57BL/6J × *M. spretus*)F_1 × *M. spretus* [2]. RECC1 was assigned by analysis of 24 individual human–rodent somatic cell hybrids ATCC (NIGMS HUMAN/RODENT BIOS Panel #2).
Database deposit information: Genbank Accession Number, U15037, U01222
Molecular reagents: A 1809-bp mouse *Recc1* cDNA (D1-12A) containing 114 bp of 5′ untranslated region (UTR) and 1695 bp of coding sequence, corresponding to the first 565 amino acids of *Recc1.*
Allele detection: A *Pst*I polymorphism was detected in mouse genomic DNA with the D1-12A probe, resulting in *M. spretus* specific restriction fragments of 4.0, 1.7, and 1.5 kb; a 7.1 kb C57BL/6J specific fragment; and a common band of 6.1 kb. In somatic cell hybrid genomic DNA digested with *Bgl*II, the D1-12A probe detected a human specific band of approximately 20 kb; mouse specific bands of 7.6, 4.8, and 1.1 kb; and hamster specific bands of 3.9, 3.5, and 2.0 kb.
Previously identified homologs: Mouse replication factor C (Genbank Accession Number, U01222 [3] and X72711 [4]), assigned by in situ hybridization to Chr 5C [4].
Discussion: Two clones (D1-12A and D1-5A) were obtained by screening a cDNA expression library from the mouse anterior pituitary thyrotropic tumor TtT-97 by the southwestern technique with a nick-translated, multimerized, double-stranded probe from nucleotides −253 to −222 of the promoter of the mouse thyrotropin β subunit gene (*Tshb*) [5]. The larger recombinant (D1-5A) includes the entire 5′ portion of the 140-kDa subunit of replication factor C cDNA and adds an additional 33 bp to the previously known sequence [3,4]. A single nucleotide change was noted at codon 254 (GCC to GTC), resulting in a valine-to-alanine substitution, possibly resulting from a polymorphism in the murine population. The ability of the *Recc1* gene product to bind DNA is not sequence specific, and it has been recently identified in two other cases by screening expression libraries by the southwestern technique [3,4]. Repeated cloning of *Recc1* from expression libraries can probably be avoided by using probes that are radiolabeled without introducing nicks. This idea is supported by the fact that a domain of Recc1 (amino acids 398–485) resembles bacterial ligases [1,3], which can bind to gapped duplex DNA.

We localized *Recc1* on mouse Chr 5 between *D5Bir9* and *Pmv11.* Synteny homology between mouse Chr 5 and human Chr 4 suggests that RECC1 would reside on Chr 4 (Fig. 1). We assigned RECC1 to human Chr 4 by analysis of somatic cell hybrids, strengthening the synteny homology in this region. Weak hybridization signals suggested the presence of related genes or pseudogenes on Chrs 15 and 17. RECC1 is part of the 5-subunit replication factor C (RFC) complex and contains regions of homology with the other subunits [1]. It is likely that these weak signals result from cross-hybridization to other subunits of the RFC complex, homologous replication factors, or ATP-binding P-loop motifs [1].

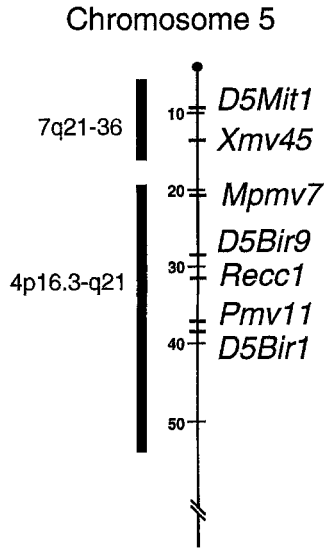

Fig. 1. The localization of *Recc1* on mouse Chr 5 is consistent with the assignment of RECC1 to human Chr 4. Haplotype analysis and minimization of crossover events was used to generate a map of mouse Chr 5. A selected set of these loci (right) were all mapped in the same cross ([2], this report). Genetic distances are in cM (left). Placement of these loci relative to the centromere was accomplished by comparing the position of *D1Mit5* with the available consensus maps ([6], GBASE). Segments of synteny homology with human Chrs 7 and 4 are indicated (black bars) based on the gene order of the chromosome report [6] and the GBASE consensus maps.

Correspondence to: S.A. Camper

Acknowledgments: We thank Dr. Arthur Gutierrez-Hartmann for his helpful discussions on the southwestern screening technique and The Jackson Laboratory for kindly providing the backcross DNA. This work was supported by National Institutes of Health grants DK36843 (E.C. Ridgway) and R01-HD30428 (S.A. Camper).

References:

1. Bunz, F., Kobayashi, R., Stillman, B. (1993). Proc. Natl. Acad. Sci. USA 90, 11014–11018.
2. Rowe, L.B., Nadeau, J.H., Turner, R., Frankel, W.N., Letts, V.A., Eppig, J.T., Ko, M.S.H., Thurston, S.J., Birkenmeier, E.H. (1994). Mamm. Genome 5, 253–274.
3. Burbelo, P.D., Utani, A., Pan, Z., Yamada, Y. (1993). Proc. Natl. Acad. Sci. USA 90, 11543–11547.
4. Luckow, B., Bunz, F., Stillman, B., Lichter, P., Schutz, G. (1994). Mol. Cell. Biol. 14, 1626–1634.
5. Vinson, C.R., LaMarco, K.L., Johnson, P.F., Landschulz, W.H., McKnight, S.L. (1988). Genes Dev. 2, 801–806.
6. Kozak, C.A., Stephenson, D.A. (1993). Mamm. Genome 4(Suppl.), S72–S87.

New localization of NCAM, proximal to DRD2 at Chromosome 11q23

M. Telatar,[1,2] E. Lange,[2] N. Uhrhammer,[2] R. A. Gatti[2]

[1]Department of Biology, Bogazici University, Istanbul, Turkey.
[2]Department of Pathology, University of California, Los Angeles School of Medicine, Los Angeles, California 90024, USA

Received: 1 August, 1994 / Accepted: 19 September 1994

Species: Human
Locus names: Neural Cell Adhesion Molecule, Dopamine D2 Receptor
Locus symbols: *NCAM, DRD2*
Map position: 11Q23
Method of mapping: Linkage analysis of 59 CEPH and 126 Ataxia-Telangiectasia families, and pulsed-field gel electrophoresis (PFGE)
Database deposit information: *NCAM:* OMIM116930, *DRD2:* OMIM126450
Molecular reagents: Southern blotting for *NCAM* and additional probes was performed as described [1–3]. The *NCAM* (CA)n repeat polymorphism was described by Telatar [4]. *DRD2* pcr primer 419 differed from the published sequence [5] by one nucleotide (that is, GGAGGGCGGTGCGTTCAT). PFGE analysis was performed as described by Uhrhammer and coworkers [6].
Discussion: In our efforts to localize the gene(s) for Ataxia-telangiectasia, we have previously constructed a linkage map spanning 100cM of 11q22-23 [1]. Two polymorphisms near the *DRD2* gene were incorporated into this map: *DRD2/TaqI* and *D11S386.* The *NCAM* gene was mapped to 11q22-23, within 500 kb of *DRD2* by PFGE [7]. Eubanks and associates [8] placed *NCAM* distal to *DRD2.* Contrary to the report by Eubanks and colleagues [8], we have linkage data and PFGE data that place *NCAM proximal* to *DRD2,* and distal to *D11S132.*

For linkage analysis, 59 CEPH families and 126 ataxia-telangiectasia (A-T) families were studied. In addition to *NCAM* and *DRD2,* seven flanking polymorphic markers in the region of Chromosome (Chr) 11q22.23 were typed: *STMY/TaqI, D11S385(CJ52.75)/MspI, D11S424(CJ52.77)/MspI, D11S132(L424)/Eco*RI and *Hin*dIII, *D11S386(CJ52.5)/TaqI, D11S144/Msp*I, and *D11S351(CJ52.208)/Msp*I. (CA)n markers at *NCAM* and *DRD2* were also typed. Three pairs of adjacent loci *(STMY–D11S385, DRD2–D11S386, D11S144–D11S351)* were combined to make more informative haplotypes. In one CEPH family, a recombination event placed *D11S386* distal to *DRD2.* This family was uninformative at NCAM/*Bam*HI. NCAM (CA)n was typed only in families that exhibited crossovers between *NCAM/Bam*HI and either *D11S132* or *DRD2–D11S386.* The two polymorphisms detected at *D11S132* were also combined into a haplotype for analysis.

Six-point location scores were computed with the computer program MENDEL [9]. With *STMY–D11S385* and *D11S424* anchored proximally, and *D11S144–D11S351* anchored distally, the cluster of *D11S132, NCAM* and *DRD2–D11S386* was tested in all six possible orders. Table 1 presents the linkage analysis results. The order *STMY/D11S385–D11S424–D11S132–NCAM–DRD2/D11S386–D11S144/D11S351* was 8.62×10^3 times more likely than the next best possible order, which placed *NCAM* distal to *DRD2/D11S386.*

Physical mapping by PFGE confirms the placement of *NCAM* between *D11S132* and *DRD2* (data not shown). The maximum distance from *D11S132* to *NCAM* was 340 kb, indicated by a common *Sfi*I fragment. A 370-kb *Sal*I fragment containing *NCAM* and *DRD2* indicate the maximum distance between these two markers. Overall, the distance between *D11S132* and *DRD2* was no larger than the distance spanned by a 650-kb common *Eag*I fragment.

Several previous reports have tried to localize *NCAM* relative to *D11S132* and *DRD2* [1,7,8]. McConville and coworkers [7] reported in 1990 that *NCAM* was within 500 kb of *DRD2,* by PFGE analysis. In 1991, Foroud and associates [1] placed *NCAM* near *D11S132,* also by PFGE analysis. More recently, Eubanks and colleagues [8] reported *NCAM* to be distal to *DRD2,* although the data supporting this assertion were not shown. We have data firmly placing *NCAM* between the proximal marker *D11S132* and the distal marker *DRD2.* Establishing the correct order of these markers is important to the positional cloning of new genes in this region.

Acknowledgments: This work was supported by grants from the Ataxia-Telangeictasia Medical Research Foundation, the A-T Medical Research Trust, the US Department of Energy 87ER60548, and National Institutes of Health Training Grant 5T32GM07104-18.

Correspondence to: R.A. Gatti

Table 1. Odds for the six possible orders of the cluster *D11S132, NCAM,* and *DRD2/D11S386* between the flanking markers *D11S424* and *D11S144/D11S351* at 11q22-23.

Order						Odds vs. best-supported order
STMY/S385	**S424**	**S132**	**NCAM**	**DRD2/S386**	**S144/S351**	**1:1[a]**
STMY/S385	S424	S132	DRD2/S386	**NCAM**	S144/S351	$1{:}8.62 \times 10^3$
STMY/S385	S424	**NCAM**	S132	DRD2/S386	S144/S351	$1{:}5.14 \times 10^4$
STMY/S385	S424	DRD2/S386	**NCAM**	S132	S144/S351	$1{:}3.76 \times 10^{13}$
STMY/S385	S424	DRD2/S386	S132	**NCAM**	S144/S351	$1{:}1.62 \times 10^{15}$
STMY/S385	S424	**NCAM**	DRD2/S386	S132	S144/ 51	$1{:}1.03 \times 10^{16}$

[a] Most likely order.