for APC and MEN IIa. I will describe our recent progress on these diseases and introduce general strategies for isolating a gene after the first linkage is detected with DNA markers on the genomic map.

**SII-2. AN APPROACH BY THE CHROMOSOME STUDY.** Shin-ichi SONTA (Inst. Develop. Res., Aichi Pref. Colony, Kasugai)

In cases with an unknown disease of dominant inheritance, chromosomes of the patient are usually analyzed at first, because cases with a certain chromosome abnormality always show abnormal phenotypes. The abnormal region of DNAs which causes genetic disorders may be various in size. They are, for instance, abnormal arrangements of DNAs, deletion of genes, and duplication of chromosome segments. The chromosome abnormalities are all morphological changes of segments distinguishable by optical microscope. The size of chromosome segments distinguishable as abnormal ones became very small by the recently improved techniques such as the high resolution banding techniques. However, individuals even with an addition or deletion of a very tiny segment of the chromosome, with the exception of a part of sex chromosomes and heterochromatic segments, have some phenotypical expression different from normal phenotypes.

Most living individuals with "balanced" structural rearrangements, which were either transmitted from the parent or occurred *de novo*, usually have no abnormal phenotype. Only a few persons with such rearrangements, however, very often show some abnormal phenotype.

Using experimental animals, we can obtain cases with "balanced" chromosome rearrangements by X-irradiation. In such "balanced" rearrangements, they may accompany the structural abnormality of DNAs and a gene at the breakpoint. If this is true, we could use the rearranged chromosome as a marker of the presence of abnormalities on DNAs and genes. The results of chromosomal observation of gametes, embryos and offspring from experimental animals with X-irradiation indicated that some cases with "balanced" rearrangements arrested at various developmental stages and some live offspring with such rearrangements evidenced some abnormal phenotypes. Furthermore, the results also indicated that some cases homozygous for "balanced" rearrangements were recessive lethal, whereas the heterozygotes have no abnormal phenotype.

These results suggest that some of the "balanced" structural rearrangements accompany abnormalities of a tiny invisible segment of the chromosome, genes or DNAs at the breakpoint and the neighboring region. The difference between dominant and recessive expression may well be due to a difference of the gene or the part of gene affected by X-irradiation.

**SII-3. USE OF TRANSGENIC MICE FOR DISSECTING THE MOLECULAR MECHANISM OF AMYLOID DEPOSITION IN FAMILIAL AMYLOIDOTIC POLYNEUROPATHY.** K. YAMAMURA,[1] S. WAKASUGI,[1] S. YI,[2] F. TASHIRO,[1] T. IWANAGA,[1] S. MAEDA,[3] K. TAKAHASHI[2] and K. SHIMADA[3] ([1]Inst. Med. Genet., [2]Dept. Pathol., and [3]Dept. Biochem. Kumamoto Univ. Med. Sch., Kumamoto)

Familial amyloidotic polyneuropathy (FAP) is an autosomal dominant disorder characterized by extracellular deposition of amyloid fibrils and by prominent peripheral and