SI-3. PRADER-WILLI SYNDROME: CONSIDERATION OF A QUESTION IN ITS CLINICAL, CYTOGENETIC AND MOLECULAR ASPECTS. Norio NIIKAWA (Dept. Hum. Genet., Nagasaki Univ. Sch. Med., Nagasaki)

Prader-Willi syndrome (PWS) is a multiple congenital anomaly/mental retardation syndrome characterized by severe muscle hypotonia in infancy, a peculiar facies, small hands and feet, hypopigmented skin, hypogonadism, poly/hyperphagia and subsequent obesity and diabetes in childhood. Because of these diverse phenotypes, PWS is thought as one of "contiguous gene syndromes." Almost all patients are sporadic, suggesting fresh mutants for autosomal dominant gene(s). Although the basic cause is unknown, 50–100% of patients show chromosome abnormality involving the 15q11.2 region. However, the cytogenetic data so far reported were diverse and controversial, *i.e.*, monosomy, disomy, trisomy, or even tetrasomy for a 15q11.2 band. Several hypotheses have been proposed, but none seems convincing to explain these complex findings. Molecular approaches were done to see a DNA deletion in PWS patients using 15q11.2-specific DNA clones as probes. However, these studies could not detect all-or-nothing results for the deletion either, suggesting that these clones would be out-side of the PWS loci. Besides PWS, it was found that patients with Angelman syndrome (AS) also have a 15q11-12 deletion, leading to another confusion.

In this symposium, the results of previous clinical, cytogenetic and molecular studies including ours on PWS and AS are reviewed. The strategy and the data of our recent approach to clone the PWS gene(s) by the microdissection/microcloning technique are also presented. With this technique, we have cloned chromosomal DNAs directly from the region at 15q11.2. Of 30 clones analyzed, one showed a one-copy density on the Southern blot of two AS patients, and the other two clones showed one-copy signal on the blots of a PWS patient, suggesting candidate clones each for the AS and the PWS genes.

SI-4. MOLECULAR ANALYSIS OF FAMILIAL POLYPOSIS COLI. Yuchio YANAGAWA and Takehiko SASAZUKI (Dept. Gen. Med. Inst. Bioreg., Kyushu Univ., Fukuoka)

An inherited cancer syndrome, familial polyposis coli (FPC) is an autosomal dominant genetic trait with high penetrance of the mutated gene and is characterized by the hundreds of adenomatous polyps with a high risk at development of colorectal carcinoma. Linkage analysis with polymorphic DNA markers demonstrated that the FPC gene is localized on the long arm of chromosome 5. In order to identify the FPC gene and analyze its functions, we have investigated the molecular mechanism of tumorigenesis in FPC.

1) We observed loss of heterozygosity in colorectal tumors from patients with FPC on 15 chromosomes and in nonpolyposis colorectal carcinomas (NPCC) on 7 chromosomes. Frequent loss of heterozygosity in colorectal carcinomas from FPC patients were observed on chromosomes 5 (24%), 14 (20%), 17 (31%), 18 (40%), and 22 (33%), and also on chromosomes 5 (32%), 14 (30%), 17 (27%), 18 (20%), and 22 (19%), in NPCC.

Loss of heterozygosity in colorectal adenoma was less than 7% on 9 chromosomes. These results suggest that tumor suppression genes for colorectal carcinogenesis may locate on the above chromosomes and that the FPC gene on chromosome 5 may be a tumor suppressor gene.

2) To identify the existence and localization of tumor suppressor genes on human