

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER  Z01 HL 00009-02 LBG
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PERIOD COVERED  
July 1, 1975 through June 30, 1976

TITLE OF PROJECT (80 characters or less)  
  
Cell Recognition and Synapse Formation

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	Marshall Nirenberg	Chief, Lab. of Biochemical Genetics	LBG NHLI
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	Hiroyuki Sugiyama	Visiting Associate	LBG NHLI
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COOPERATING UNITS (if any)  
  
Behavioral Biology Branch, NICHD

LAB/BRANCH  
Laboratory of Biochemical Genetics

SECTION  
Section on Molecular Biology

INSTITUTE AND LOCATION  
NHLI, NIH, Bethesda, Maryland 20014

TOTAL MANYEARS: 2.2	PROFESSIONAL: 2	OTHER: .2
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SUMMARY OF WORK (200 words or less - underline keywords)

Long range objectives are to define reactions which are required for synapse formation and for transmission of information from cell to cell.

## Project Description:

Major Findings: Since normal neurons do not divide, clonal lines of neuroblastoma cells and somatic cell hybrids derived from neuroblastoma cells were generated and characterized with respect to receptors, neurotransmitters, action potential ionophores, and other properties which are required for synaptic communication. Fusion of clonal neuroblastoma cells with glioma cells yielded clonal hybrid cell lines which synthesize, store and excrete acetylcholine; properties which are not expressed by the parental cell lines. During the past year cells from one hybrid line were found to form synapses with cultured striated muscle cells. Synapses between hybrid cells and muscle cells closely resemble the synapses between normal motor neurons and striated muscle before they are fully developed. Under appropriate conditions, hybrid cells established synaptic connections with almost every muscle cell tested; thus, synapses are synthesized in abundance. Marked differences were observed in the efficiency of transmission across different synapses. Axonal activities which were found to be regulated include choline acetyltransferase, acetylcholinesterase,  $\text{Na}^+$  action potential ionophore specific activities, and the rate of choline transport into cells.

Eight species of receptors have been found thus far with the hybrid cell line which forms synapses. Receptor mediated shifts in cAMP levels, cGMP levels and membrane potentials have been identified and characterized. Thus the foundation has been laid for studies on the effects of receptor-mediated reactions on synaptic transmission. In addition, more than 100 cell lines which synthesize acetylcholine have been obtained and are being studied to determine that some cell lines are defective with respect to synapse formation.

Significance to Biomedical Research: This is the first time that clonal cells of neural origin have been shown to form synapses. Thus the set of genes which are required for synapse formation are expressed in this cell line. The model system which has been established affords extraordinary opportunities to define synapse formation reactions and properties and correlate biochemical events with developmental and electrophysiological phenomena.

Proposed Course: Current studies focus on determining the reactions which are required for synapse formation and factors that regulate these reactions.

## Publications:

1. Greene, Lloyd A., Shain, William, Chalazonitis, Alcmene, Breakefield, Xandra, Minna, John, Coon, Hayden G. and Nirenberg, Marshall: Neuronal properties of hybrid neuroblastoma x sympathetic ganglion cells. Proc. Natl. Acad. Sci. USA 72: 4923-4927, 1975.

2. Chalazonitis, A., Greene, L.A. and Shain W.: Excitability and chemosensitivity properties of a somatic cell hybrid between mouse neuroblastoma and sympathetic ganglion cells. Exp. Cell Res. 96: 225-238, 1975.

3. Nelson, Phillip, Christian, Clifford and Nirenberg, Marshall: Synapse formation between clonal neuroblastoma x glioma hybrid cells and striated muscle cells. Proc. Natl. Acad. Sci. USA 73: 123-127, 1976.
4. Nirenberg, Marshall W.: Coding of neural information by neuroblastoma cells. In: Talwar, G. P. (Ed.): Regulation of Growth and Differentiated Function in Eukaryote Cells. New York, Raven Press, pp. 537-539, 1975
5. Thompson, Edward J., Griffith, James M., Glazer-Schoenberg, Deverera and Nirenberg, Marshall W.: An improved method for extracellular recording of action potentials from single cultured neuroblastoma cells. Med. Biol. Eng. 13: 104-106, 1975.
6. Hamprecht, Bernd, Kemper, Wayne and Amano, Takehiko: Electrical response of glioma cells to acetylcholine. Brain Res. 101: 129-135, 1976.