chemotaxis, movement, thermotaxis, osmotic avoidance, egg-laying, touch sensitivity, and in the synthesis and degradation of neurotransmitters. Obtaining such mutants is a first step in trying to understand the molecular basis of the functioning and development of the nervous system.

The work on touch-insensitive mutants, which has been carried out by Chalfie and Sulston, illustrates very well the approach to genetic dissection of neural development and nerve cell differentiation. There are six touch receptor cells, which are located in the head, mid- and tail regions of the body and mediate the worm's response to gentle tactile stimulation. All six have long processes that run just below the cuticle and act as mechanoreceptors.

Chalfie and Sulston have been screening for specifically touch-insensitive mutants and have by now listed 250 mutations in 15 genes that affect this behavior. Mutations in eight of these genes result in visible defects in the touch neurons, whereas mutations in the other seven produce touch insensitivity in the absence of visible defects in the nerve cells.

Four of the eight genes affect ultrastructural features of the cells, including the organization and number of microtubules and the presence of a characteristic extracellular material known as mantle. A mutant defective in another gene has

The Other T-Cell Receptor Gene

During the past year or so immunologists have achieved a long-sought goal—the identification of the receptor molecules by which T cells recognize antigens. Knowledge of the structure of this receptor is essential for an understanding of how T cells perform their immune functions, which include both killing cells they recognize as foreign and controlling the activities of other immune cells, including the antibody-producing B cells.

The T-cell receptor is now known to consist of two different protein chains, both of which are structurally similar to antibody proteins. In addition, several months ago two groups reported that they had cloned receptor genes. One was cloned from mouse cells and the other from human cells, but both turned out to code for the same chain, which has been designated β (*Science*, 25 May, p. 859). The α chain remained elusive, until now that is. Susumu Tonegawa, Herman Eisen, and their colleagues at the Massachusetts Institute of Technology have reported the cloning of what appears to be an α-chain gene from a line of mouse T cells.* They have also cloned a β-chain gene from the same cell line.

The MIT workers used the subtraction method of cloning, which Mark Davis of Stanford University School of Medicine and Stephen Hedrick of the University of California at San Diego developed and used to clone the mouse β-chain gene. That gene may have turned up first, Tonegawa suggests, because there are five to ten times more copies of its messenger RNA (mRNA) than of α-chain mRNA's in T cells. The MIT workers may have found the α-chain clone because they screened a very large number of clones, 100,000 compared to the 5,000 screened by Davis and Hedrick.

The evidence that it is an α-chain gene is still indirect, Tonegawa notes. The gene is expressed specifically in T cells, as predicted for a T-cell receptor protein, and has undergone a rearrangement. Complete T-cell receptor genes, like those of antibody genes, are assembled during maturation of the cells by joining shorter DNA segments. In addition, determination of the nucleotide sequences of the proposed α and β clones has shown them to be different. "The predicted protein sequence of the α chain has homology to immunoglobulins [antibodies] as the β chain does, and to about the same extent," Tonegawa says, "but it is very different from the β chain." About 30 percent of the amino acids of the α and β chains are identical.

The overall organizations of the two chains are very similar to each other, however, and to those of antibody proteins. Both have molecular weights of about 33,000. They each contain a short region that extends into the cytoplasm of the cell, a membrane-spanning segment, and a large extracellular segment. Both have cysteine residues just outside the transmembrane region that might form the disulfide bond that holds the chains together. As in antibody chains, the extracellular segment consists of a constant region, which is the same for all chains of the same type, and a variable region, which differs from molecule to molecule and is involved in antigen recognition. The constant region of the MIT β-chain clone, which is from a cytotoxic cell line, and that of the Hedrick and Davis clone, which is of helper T-cell origin, are essentially identical, Tonegawa points out, but the two genes use different variable region coding segments.

At least five gene segments coding for β-chain variable regions have been identified and there may be many more. The repertoire of α-chain variable regions may be more limited. "There appears to be only a few for an entire population of cytotoxic T cells," Tonegawa explains. Some variability can be generated, however, in the joint between the variable region coding segment and that for the J (for joining) segment, which in antibody light chains lies between the variable and constant gene segments. Antibody heavy chains, and the β chain of the T-cell receptor, also contain a fourth coding segment, designated D for diversity. A D segment has not yet been identified for the α chain.

The T-cell receptor only recognizes a foreign antigen in conjunction with a histocompatibility molecule, which is a marker for self. Partly because of the apparently limited variability of the α chain and partly because there are indications that the variable regions of the two receptor proteins may interact less closely than the variable regions of light and heavy antibody chains, Tonegawa suggests that the α chain primarily recognizes the histocompatibility molecule, whereas the β chain primarily interacts with the foreign antigen, although he stresses that more work will be needed to confirm this suggestion. Analysis of the T-cell receptor, which was already moving rapidly should proceed even faster if both genes are now in hand.

—JEAN L. MARX

*H. Saito, D. M. Kranz, Y. Takagaki, A. C. Hayday, H. N. Eisen, S. Tonegawa, *Nature (London)* **309**, 757 (1984).