Scientists collaborate on study using plants to produce secretory antibodies

London, U.K., and La Jolla, CA. May 5, 1995 — Scientists from the Department of Immunology at Guy’s Hospital, London and the Department of Cell Biology/Division of Plant Biology at The Scripps Research Institute (TSRI), La Jolla, California, have developed a new approach to the production of secretory antibodies, as reported in the current issue of *Science*.

Secretory immunoglobulin A (SIgA) is the most abundant form of immunoglobulin in mucosal secretions, where it forms part of the first line of defense against infectious agents. According to TSRI scientist Mich Hein, Ph.D., “It has been very difficult generating secretory IgA monoclonal antibodies, so producing these molecules with plants is important both for advancing science and for potential therapeutic purposes.” The previous problems in producing SIgA have been due to the complicated nature of the immunoglobulin; the process requires plasma cells expressing the dimeric molecular form of IgA as well as epithelial cells expressing polymeric immunoglobulin receptor.

Accordingly, the two groups, led by Julian K-C. Ma, Ph.D., in London, Mich Hein, Ph.D., and Andrew Hiatt, Ph.D., in California took another approach. Four genetically manipulated *Nicotiana tabacum* plants were generated, each expressing one of the four constituent protein chains of SIgA - a murine monoclonal antibody kappa chain, a hybrid immunoglobulin A-G antibody heavy chain, a murine joining chain and a rabbit secretory component. Successive

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sexual crosses between these plants and filial recombinants resulted in plants that expressed all four protein chains simultaneously. These chains were assembled into a functional secretory immunoglobulin that recognized the native streptococcal antigen, cell surface adhesion molecule.

In plants, single cells are able to assemble the secretory antibodies, while in mammals, two different cell types are required (as noted above). Transgenic plants thus may be suitable for large-scale production of recombinant secretory immunoglobulin A for passive mucosal immunotherapy. According to Julian Ma, Ph.D., “Now that it will be possible to generate secretory antibodies in large quantities, we can contemplate passive immunization against a number of human pathogens that colonize mucosal surfaces. Another exciting finding has been that plants can assemble large, complex proteins like SIgA very accurately. This holds great promise for the future use of transgenic plants as bioreactors for recombinant proteins.”

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