

This Week's Citation Classic

Tomasi T B, Jr., Tan E M, Solomon A & Prendergast R A. Characteristics of an immune system common to certain external secretions. *J. Exp. Med.* **121**:101-24. 1965. [Div. Exper. Med., Univ. Vermont, Coll. Med., Burlington, VT and Rockefeller Institute, New York, NY]

Abstract of techniques: Isolation of proteins from human saliva, milk, and serum by salt precipitation, ion exchange, and molecular sieve chromatography. Fluorescent antibody examination of tissues. *In vitro* culture synthesis of proteins using ¹⁴C leucine incorporation. Radiolabeling of IgA with iodine and injection into normals to quantitate distribution in serum and secretions. Measurement of specific antibody to blood group antibodies in different classes using hemagglutination and absorption with class specific antisera. [The *SCI*[®] indicates that this paper has been cited over 695 times since 1965.]

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"This paper was the first to suggest the concept of an immune system common to mucosal fluids. It described in detail the chemical differences between serum and secretory antibodies. I am pleased that the work has been verified and extended in other laboratories and has stood the test of time. Other workers have showed its potential importance as a 'first line of defense' against potentially pathogenic microorganisms and the importance of stimulating this system in immunization against viruses and bacteria that enter the body via mucous membranes. More recently, evidence has been presented that the secretory system, as it is now called, may regulate the absorption of nonviable materials that are inhaled or ingested and that abnormalities of the mucosal system may occur in certain human diseases.

"You might be interested in the evolution of this work. Halsted Holman at Rockefeller University was examining the gastric secre-

tions from patients with protein-losing enteropathies and found on immunological analysis that there was a good deal of gamma globulin in the fluids from these patients and also in normal controls. It occurred to me that perhaps some of these proteins were derived from swallowed saliva, and some weeks later I expectorated into a beaker and examined the whole saliva by gel diffusion using antialbumin and anti-gamma globulin antisera. Roughly quantitated by eye there appeared to be considerably more gamma globulin than albumin in saliva. This was unexpected if one assumed that the proteins in saliva were derived from serum by simple transudation. About that time I went to the University of Vermont, and during my first year a third year medical student, Sheldon Zigelbaum, now a psychiatrist in Boston, wished to do a summer research project in my lab. He was also a dentist, and the closest study I could think of to a 'dentally oriented' project was the observation on saliva. I suggested that he try to repeat my former observation and do more accurate quantitation of the proteins. With the assistance of a superb technician, Dolores Czerwinski, we showed by quantitative precipitation that there was four times more gamma globulin in normal parotid fluid than there was albumin. We subsequently continued this work using specific antisera and showed that the major gamma globulin in saliva and in most other external secretions was IgA.¹ These findings were first reported at the interim meetings of the Arthritis Association in 1963. I then went back to Rockefeller University, and it was there that I examined in a more sophisticated fashion, using methods involving *in vitro* synthesis, the fluorescent antibody technique, transport of labeled proteins from serum into secretions, and the measurement of specific antibodies and their classes in secretions, all with great assistance from my coauthors who were working primarily on other problems in Kunkel's laboratory. It is gratifying that this work has formed the basis for what is now an active area, and I think holds even more potential for the future."

1. Chodirker W B & Tomasi T B, Jr. Gamma-globulins: quantitative relationships in human serum and non-vascular fluids. *Science* **142**:1080-1, 1963.