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This Week's Citation Classic®

Pereira M E A, Kabat E A, Lotan R & Sharon N. Immunochemical studies on the specificity of peanut (*Arachis hypogaea*) agglutinin. *Carbohyd. Res.* 51:107-18, 1976.
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This paper describes the fine sugar specificity of the anti-T lectin from peanut. Quantitative precipitin and quantitative precipitin inhibition assays were employed to demonstrate that the lectin is most specific for Galβ1-3GalNAc and Galβ1-4GlcNAc structures. The presence of sialic acid on those structures blocked lectin binding. Therefore, the peanut lectin is a useful tool to ascertain the sialylation of glycoconjugates, whether in solution or on the surface of cells. [The *SCI*® indicates that this paper has been cited in more than 200 publications.]

Of Peanuts and Lectins

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My interest in lectins started in 1964 when I was a first-year medical student in Fortaleza, Ceará, Brazil. The local medical school library subscribed to a few international journals such as *Lancet*, which were always delivered several months late. But I read them avidly, anyway. One day I saw a paper showing lymphocyte stimulation by antigens and by phytohemagglutinin,[1] a lectin from red kidney beans. The idea that lectins could trigger the multiplication of lymphocytes (then thought by many to be dead-end cells) was very appealing to me. In the summer of 1968 I took a three-day bus trip to Rio de Janeiro to gain hands-on experience with lymphocyte stimulation by lectins. There, under Marcello Barcinsky's guidance, I first saw leuko- and hemagglutination. After I came back to Fortaleza, I wrote my first paper on lectins.[2] In 1971 I became a postdoctoral fellow in Elvin A. Kabat's laboratory at Columbia University. My project was to purify and characterize the lectin from *Lotus tetragonolobus*. It allowed Kabat to teach me basic quantitative immunochemistry.

At that time, the concept of lectins as specific sugar-binding reagents was not well understood by most biologists. Then the world suddenly changed, thanks to a provocative review article by N. Sharon and H. Lis.[3] Although the same group subsequently wrote many other reviews on lectins, to me this one remains the best because of its simplicity.

In 1975, I received a great gift: several milligrams of lyophilized peanut agglutinin (PNA). It had been purified by R. Lotan in Sharon's lab at the Weizmann Institute and brought to New York by Kabat. Sharon and Kabat had decided to determine the fine sugar specificity of PNA by using the battery of oligosaccharides and glycoproteins available in Kabat's lab. I was just lucky to be the one chosen by Kabat to do the project. I completed the work in just a few months. The paper probably became a *Classic*® because, as the importance of sialyl and galactosyl residues were recognized in biological systems, PNA binding became a useful method to detect desialylation of glycoconjugates. PNA was also popular because of the demonstration by Y. Reisner, in Sharon's lab, that the lectin is useful for the fractionation of mouse and human thymocytes into immature and mature cells.[4]

PNA changed my life. Soon after I became an independent investigator, we discovered sialidase (neuraminidase) in *Trypanosoma cruzi*,[5] the cause of Chagas' disease, an incurable disease in Latin America. It all started when Arnaldo Andrade, a friend and classmate from medical school, and I mixed *T. cruzi* with human erythrocytes to test whether the red blood cells would become desialylated. Desialylation was detected by PNA hemagglutination! If we had attempted to determine free sialic acid by the periodate-thiobarbituric acid assay, which is very insensitive, and not by PNA, we would not have detected the enzyme. This discovery led to my first NIH grant, which has been successfuly renewed several times—knock on wood! The neuraminidase, now known as trans-sialidase, is currently studied throughout the world.[6]

So, I cannot take much credit for having the PNA paper as a *Citation Classic*®: It all belongs to Sharon and Kabat. I was just lucky to have read papers on lectins when I was a medical student and to be in Kabat's lab at the right time. Otherwise, I might not have appreciated the importance of PNA as a detector of sialylation in glycoconjugates.

1. **Elves M W, Roath S, Taylor G & Israels M C G.** The in-vitro production of antibody lymphocytes. *Lancet* 1:1292-3, 1963.
2. **Pereira M E A.** A transformação linfocitaria in vitro (Lymphocyte transformation in vitro). *Pesquisa Medica* 3:56-85, 1966.
3. **Sharon N & Lis H.** Lectins: cell agglutinating and sugar-specific proteins. *Science* 177:949-59, 1972. (Cited 1,420 times.)
[See also: **Sharon N & Lis H.** Citation Classic. (Barrett J T, ed.) *Contemporary classics in the life sciences. Volume 1: cell biology*. Philadelphia: ISI Press, 1986. p. 57.]
4. **Reisner Y, Linker-Israel M & Sharon N.** Separation of mouse thymocytes into subpopulations by the use of peanut agglutinin. *Cell Immunol.* 25:129-34, 1976. (Cited 520 times.)
[See also: **Reisner Y.** Citation Classic. *Current Contents'/Life Sciences* 30(44):19, 2 November 1987.]
5. **Pereira M E A.** A developmentally regulated neuraminidase activity in *Trypanosoma cruzi*. *Science* 219:1444-6, 1983.
6. **Hall B F, Webster P, Ma A K, Joiner K A & Andrews N W.** Desialylation of lysosomal membrane glycoproteins by *Trypanosoma cruzi*: A role for the surface neuraminidase in facilitating parasite entry into the host cell cytoplasm. *J. Exp. Med.* 176:313-25, 1992.

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