

This Week's Citation Classic

Inbar M & Sachs L. Interaction of the carbohydrate-binding protein concanavalin A with normal and transformed cells.

Proc. Nat. Acad. Sci. US 63:1418-25, 1969.

[Department of Genetics, Weizmann Institute of Science, Rehovot, Israel]

This paper demonstrated that the interaction of the carbohydrate-binding protein concanavalin A (Con A) with membranes of intact normal and malignant transformed cells induces an agglutination of the transformed cells exclusively. Furthermore, it was also shown that this specific agglutination can be reversed by competition with the carbohydrate α -methyl-D-glucopyranoside that specifically binds to Con A. [The SCI® indicates that this paper has been cited over 650 times since 1969.]

Michael Inbar

Department of Cell Biology
Miles-Yeda Ltd. Kiryat Weizmann
Rehovot 76326
Israel

February 10, 1982

"After one year of studying the *in vitro* transformation of normal cells induced by X ray in Leo Sachs's laboratory at the Weizmann Institute of Science, it became necessary to change the subject of my PhD thesis and make other plans. It is evident that such a situation does not usually create a very friendly environment; however, after few, but long, discussions with my supervisor, he suggested that I find a new subject for my doctoral research.

"The work of M. Abercrombie, E.J. Ambrose, L. Weiss, A.B. Pardee, and others in the early-1960s suggested that the phenomena of malignant transformation, cell invasion, and metastasis may depend on the structure of the cell surface membrane. However, this area of research, known today as cellular membranology, was at that time in its early stages of development mainly due to the fact that not too many biochemical tools were available to study the complex structure of cell membranes (do we now have better tools?).

"In retrospect, the use of plant lectins as markers to study carbohydrate-containing

membrane receptors on cell surfaces was initiated by J.C. Aub and co-workers¹ when they found that a lipase preparation from wheat germ agglutinates malignant cells exclusively. However, only a few years later, M.M. Burger and A.R. Goldberg² found that this differential agglutinability of normal and malignant cells is due to the presence of an agglutinin existing as an impurity in the lipase preparation. The purified wheat germ agglutinin (WGA) was found to be a glycoprotein that binds to the carbohydrate N-acetyl-glucosamine. These studies, together with a great deal of help from A.J. Kalb and J. Yariv, members of our institute who at that time were studying protein-carbohydrate interactions, led me to 'rediscover' the well-known protein concanavalin A (Con A), which was first isolated in a purified form from jack bean in 1936 by J.B. Sumner and S.F. Howell.³ The next logical step was therefore to test the ability of Con A to interact with membrane receptors and agglutinate mammalian cells. This simple experiment has generated a tremendous amount of work since 1969, reaching a peak of interest with the publication of a book entitled *Concanavalin A as a Tool*.⁴

"I believe now that my initial work with Con A, together with the great deal of support I received from A. Dorfman of the University of Chicago, introduced the general concept that the interaction of lectins with membrane receptors in a reaction similar to the formation of an antigen-antibody complex is indeed a useful tool to study carbohydrate-containing membrane receptors in mammalian cells. Furthermore, I would also like to take the liberty of thinking that my first publication became a *Citation Classic* because of the many scientists who later used Con A as a tool in many different cellular systems and felt obligated to refer to our paper in which Con A was first used for such an application. It is also possible to assume that this paper was cited many times because the study on the interaction of Con A with mammalian cells was indeed a real 'push' for the concept of the dynamic structural organization of biological membranes."

1. Aub J C, Tieslan C & Lankester A. Reactions of normal and tumor cell surfaces to enzymes. I. Wheat-germ lipase and associated mucopolysaccharides. *Proc. Nat. Acad. Sci. US* 50:613-19, 1963.
2. Burger M M & Goldberg A R. Identification of a tumor-specific determinant on neoplastic cell surfaces. *Proc. Nat. Acad. Sci. US* 57:359-66, 1967.
3. Sumner J B & Howell S F. The identification of the hemagglutinin of the jack bean with concanavalin A. *J. Bacteriology* 32:227-37, 1936.
4. Bittiger H & Schnell H P, eds. *Concanavalin A as a tool*. London: Wiley, 1976. 639 p.