responding gliomas are not readily transplantable[5-7]. These observations suggest that ENU-induced rat gliomas are strongly antigenic while the schwannomas are weakly or not antigenic[8,9].

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Résumé. L'éthylnitrosurée, injectée à des rates portantes, produit des tumeurs par voie placentaire dans le système nerveux de leurs descendants. In vitro, les lymphocytes spléniques des rats atteinst de gliomes furent cytotoxiques envers les cellules autologues de ces tumeurs, mais inactifs envers les cellules des schwannomes autologues. L'infiltration a eu lieu dans quelques gliomes, mais ne s'est pas produite dans le schwannomes.

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COGITATIONES

Are There any Nonspecific Large Molecule-Large Molecule Interactions?

In 1960[1] I was concerned with convincing my readers that some of the 'nonspecific' lectins extracted from plant seeds (invertebrate lectins had not yet been studied) were not so nonspecific after all. Writing to-day I should say, 'We have discovered the specificity of some plant lectins; here is some of the evidence'.

It is well known that the first lectin found to be blood group specific was the anti-A from Lima beans[2,3]. Elsewhere I have described the train of thought that led me to this discovery[4]. This lectin also precipitated specifically with blood group A substance. By studying the inhibition reactions of anti-A lectins, MORGAN and WATKINS[5] were able to conclude that the terminal unit of the polysaccharide chain determining the specificity of the A substance was N-acetyl-D-galactosamine. Since then a number of lectins, plant and invertebrate animal, have been studied, and SHARON and LIS[6] give a list of 18 such agglutinins that have been obtained in highly purified form. In the case of 15 of these the sugar specificity (presumably the terminal unit of the polysaccharide grouping with which they react) has also been determined. In addition to the L-galactose listed by SHARON and LIS as reacting with the lectin of *Ricinus communis*, BOYD and WASZCZENKO-ZACHARCZENKO[7] found 3 other sugars of Mäkelä's group 2 to inhibit as well or better. Sugars of group 3, however, which inhibited the 'nonspecific' lectin of *Bauhinia purpurea* var. *alba*, did not inhibit the *Ricinus* lectin at all. Therefore, although the complete structures of the receptors for these two lectins have not been elucidated, it is clear that each has a specificity, and that the two specificities are different.

Lectins probably came to be classified as 'nonspecific' because ealier work in immunology, always preeminently an applied science, had led to a narrow definition of specificity. Antibodies were considered useful if they reacted exclusively, or nearly so, with just 1 antigen. When it was attempted to produce immune agglutinins for the blood group antigens such as A, B, M, and N, the first step after injecting and bleeding the animals was to absorb out of the serum the 'nonspecific' agglutinins that reacted with all human bloods, leaving the agglutinins specific for A B, etc. The unwanted 'unspecific' agglutinins, more numerous and more abundant, which doubtless possess their own specificities, were labeled 'non-specific', absorbed out, and thrown away.

The haemagglutinating action of *Ricinus* extract was described before erythrocyte agglutinins were demonstrated in animal blood[4], soon after specific bacterial agglutination had been discovered. But *Ricinus* extracts agglutinate the erythrocytes of human beings of all blood groups, and of many species of animals[4], so this agglutinin was labeled 'nonspecific', and until recently little work was done on it, although LANDSTEINER had found it to agglutinate pigeon erythrocytes much better than horse erythrocytes. LANDSTEINER was well acquainted with the earlier work with plant agglutinins, and carried the work forward himself. He wrote a paper on 'Pflanzliche Hämagglutinine' which reached the stage of page proof, but was never published[8].

The haemagglutinating action of lectins is not the only interesting thing about them. Certain lectins are mitogenic[6], and this property has played a part in the important studies on the relationship between chromosome abnormalities and human diseases. Lectins have been found that are specific for tumor cells[6], greatly increasing interest in these substances. See also the recent Conference at the N.Y. Academy of Sciences[9].

Why do I now say it should have been obvious that all lectins have a specificity? Basically, because I think that lectin-antigen reactions, like antibody-antigens, involve surface configurations of limited size, as in fact do nearly all large molecule-large molecule interactions[10]. Actually it is difficult to imagine how 2 large molecules of the same overall charge could interact in any other way. Since these

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configurations are of limited size, and are built up from a limited number of basic units, their possible variety, though large, is finite. Various workers have suggested that the number of different antibody specificities is limited. HAUROWITZ[11], estimated that not over 50,000 different antibodies exist, and TALMAGE[12] proposed making do with 5,000.

The specificity of a lectin is evidently due to the fact that one or more (usually several, it seems) of its surface configurations is complementary to a configuration that occurs one or more times on the surface of a polysaccharide or a protein molecule. It is not to be expected that a lectin will possess a configuration complementary to a configuration that appears in all polysaccharides or all proteins, which might make it indeed nonspecific.

These arguments are supported by several lines of evidence: The work of KABAT[13] indicates that the specific determinant groups of polysaccharides are made up of only about 6 monosaccharide residues. The complementary configuration in the corresponding antibody or lectin would therefore be of similar size. LANDSTEINER's experiments with di-, tri- and polypeptides as haptens[14] indicated that polypeptides containing 5 or 6 amino acids were about as large as the antibody-forming mechanism cared to recognize as a single determinant. SPRINGER and DESAI[15] found the specific determinant recognized by the anti-H(0) lectin of the eel to be a portion of a single monosaccharide. It is hard to believe that the specifically reactive structure in this lectin is very complicated.

The specifically reactive groups in other lectins likewise seem to be of limited size. MATSUBARA and BOYD[16–19] found that relatively minor chemical alteration of a lectin could alter its specificity considerably. They found[18] that phenylazobenzoylation of the Lima bean and *Sophora japonica* greatly increased the anti-A activity. Examination of pronase digests of these modified lectins showed that the peptide containing the PhAB residue was composed of only 3 or 4 amino acids: not proof, to be sure, but suggestive.

ETZLER and KABAT[20] found that the purified lectin of *Dolichos biflorus* was specific for α-linked D-GalNAc, although they did not establish the exact size of the complete reactive group in the antigen, and HAMMARSTRÖM and KABAT[21] found that the purified lectin of *Helix pomatia* precipitated with macromolecules having terminal α-linked D-GalNAC, but not with those having β-linked D-GNAc end groups. PORETZ and GOLDSTEIN[22] reported that in the purified concavalin A molecule there are present binding loci complementary to the 1,5-anhydro-2-deoxy-D-arabino-hexitol or the arabinofuranosyl ring systems. All these observations combine to suggest that the specifically reactive group in the lectin is relatively small.

Considering all of the above facts, I venture to suggest that, aside from purely physical chemical processes such as the precipitation of proteins with normal isoelectric points by the basic histones, there are no nonspecific large molecule-large molecule interactions.

Zusammenfassung. Es wird diskutiert, ob die Wirkung pflanzlicher Hämagglutinine als spezifisch oder unspezifisch zu bezeichnen sei und festgestellt, dass eigentlich fast alle Reaktionen zwischen Molekülen mit grossem Molekulargewicht spezifisch sind.

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THEORIA

The Possible Effect of Meteorological Stress on Cancer and its Importance for Psychosomatic Cancer Research

In any adult multicellular organism there is a close interrelationship between cell growth, cell metabolism and the state of the central and autonomic nervous systems. Disturbances in the nervous balance are reflected in hormonal disturbances causing a dysfunction of enzymatic mechanisms, tissue functions, antibody formation, etc. It could affect also the histological structure of nerve ganglia and fibres (KHAZANO, 1937).

Experimental studies, particularly in the USSR (PETROVA, 1945; KAVETSKY, 1951; KAVETSLY, TURKEVICH and BALITSKY[1]) and in the USA (e.g., CORSON[2]) have shown that disturbances in the higher brain centres could trigger and accelerate neoplastic diseases. Several physiological mechanisms are involved.

Overstimulation of the brain centres and of the cerebral cortex creates a weakening of the cortical functions, affecting the thermoregulatory function of the hypothalamus, the functions of the rhinencephalon or emotional brain (PRICK[3]), of the pituitary, thyroid and adrenal gland and of the thymus, essential for the production of lymphocytes and development of adequate

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