Candida albicans and Our Body's Endogenic Defenses

Reciprocal Actions With the Immune Functions of the Body

by Dipl. Biologist Joachim Hartmann

Semmelweis-Institut GmbH

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The following elaborations form a background to the development of the SANUM preparations ALBICANSAN and EXMYKEHL, which hold the promise of a successful biological therapy for widely spread mycoses in their diverse appearance forms. The decisive factor for the manifestation of a Candida infection, where there is a contact between a mammalian organism and cells of the yeast fungus, is always the result of interactions between the virulent factors of the yeast and the endogenic defense mechanisms of the host. Particularly decisive for the manifestation of an infection is the capacity of the Candida cells to attach themselves and adhere to the host cells. This initial step depends on the surface of the cellular wall of the yeast cells, as well as on possible receptors on the body cells, which are able to interact with the yeast structures.

Among the three main constituents of the Candida albicans cell wall, the poly-saccharides glucan and chitin serve the structural maintenance and shaping of the yeast cells. The third polymer mannan consists of mannose units, with the structural chain occasionally branching into side chains, as is the case with glucan. The poly-saccharide is tied to proteins of the cellular wall and is, therefore, called a manno-protein. The glycoprotein has very important functional properties in the manifestation of Candidiasis. Namely, it effects the adherence of Candida albicans cells to the host cells. Diverse test models have been in use in order to study the adherence of Candida albicans to human cells *in vitro*.Under observation were keratinozytes, mucous membrane cells of the mouth, uroepithelial cells, and vaginal epithelial cells, fibrin thrombi, as well as artificial materials for simulation of prostheses.

Influences Toward Adherence of Candida cells

The transformation from the yeast form into the mycelial form can be proven electron-optically through the morphologic changes in the subtle structure of the cell wall. Herein, a fibrin layer of manno-protein gets deposited on the outermost layer of the cell wall. Under certain culture conditions, the extent of fibrin formation is so large that they are excreted into the surroundings. For example, a high concentration of saccharose effects such a fibrin excretion. Likewise, the fibrin layer has been discovered to be an important factor in the adherence of Candida albicans to host cells. If one isolates Candida cells from the mucous membrane of Candida patients through a mouth swab, the yeast cells show a strong layer of fibrin. Here, on the level of cellular morphology, is shown why a high sugar concentration in the mouth intensifies the Candida invasion.

Cell wall manno-protein, isolated from Candida albicans, attaches itself onto the diverse cell receptors. However, if the poly-saccharide is first enzymatically split (with alpha mannosidase), no adherence to human cells takes place. Interestingly, mannoprotein has the capacity for complement activation. This enzyme system, being a component of the immune defense, complements the immunologically specific effects of the antibodies:

- through its function of cellular activation, zytolysis and opsonization;
- through attachment of opsonins (complement factors).

Through these, cells become phagoytable. From among the many components of the complement reactions cascade, the manno-protein of Candida albicans reacts with the metabolic products of the third component (iC_3b, C_3d).

These complement receptors are especially strongly active in virulent strains of Candida albicans, which correlates here with the capacity for developing the mycelial phase. Namely, it has been noted that the adherence of Candida albicans to epithelial cells happens considerably stronger in the fungal phase than in the yeast form. Certain surface antigens are developed only on fungal mycelia during their colonization of human tissue. Factually, the complement receptors also were found in much larger numbers on the surface of the mycelial form.

As a hypotheses for the mimicking function of physiologically complement receptors through Candida albicans, it has been formulated: **Through the formation of complement components, their later decomposition is facilitated; by it, complement capable of reactions is withdrawn from service.** The linkage complement components and complement receptors on the Candida cells is based on a lectin like effect of the complement component C3. Lectins are proteins with recognition areas for special

poly saccharide structures. In this way, again, the special function of the Candida manno-protein is confirmed.

Phases and Factors of Immunologic Defenses

The cellular immune defense is of central importance in preventing Candida albicans. Triggered through certain antigenic surface structures of the Candida cells, the T-Lymphocyte population gets stimulated, effecting the following by the excretion of Lymphokines:

1. The chemotactic attraction of circulating monocytes (macrophages and antigen presenting cells);
2. The activation of tissue macrophages for intensified phagocytosis;
3. The blocking of the removal of macrophages from the site of infection.

A well functioning immune defense is able to damage both the yeast form and the mycelial forms of Candida albicans through phagocytosis. However, once a Candidiasis has settled in, the effectiveness of the macrophages is considerably restricted. Apparently, the numerous complement receptors present on the mycelial surface effect the development of complement bridges between several Candida hyphae so that these larger aggregates cannot easily be phagocytized. The bridging construction occurs between already opsonized Candida cells, which have already been tied through the complement factor C3 via acceptor, and free receptors of Candida cells for the complement factors iC_3b and C_3d. Thereby, complement is again removed, for which the receptors an the macrophages compete. This, too, limits the possibility of phagocytosis. The recognition of opsonized Candida cells by macrophages and granulocytes is blocked.

The macrophages which kill off and digest the phagocytized microorganisms mainly by the enzymes acid hydrolase and peroxidase, contained in their lysosomes - receive support in their activities from the neutrophil granulocytes. The latter contain as their effective substance the enzyme myeloperoxidase, which halogenates the Candida proteins in the presence of H_20_2 and halogen anions. Myeloperoxidasis preferably ties up with the outer manno-protein of the Candida cells, which, however, escape these attacks by a type of "mimicry." In this way, these phagocytized Candida hyphae excrete substances, which settle on the Candida receptors of the granulocytic surface, thus blocking the essential task, namely the binding of granulocytes of the still living mycelia.

On the level of humoral immunity, Candida albicans escapes the defensive mechanisms through the yeast mycelial dimorphism. During this morphogenesis, not only the outer cell wall layers, but also deeper layers are chemically rebuilt or expelled. Therefore, the antibodies directed against the yeast forms can no longer "recognize" the pathogen, which now appears as fungal mycelia, and they lose their protective function.

The adaptive mechanisms of Candida albicans to the immune defenses of its human host are, as presented, very subtle and extensive. The yeast fungus has characteristics, which evade nearly all defense attempts directed against it an every level. The nearly "intelligent" binding and counter binding concept on the level of complement and Candida complement receptors, occurs only in the especially virulent species of Canida albicans, but not in the less pathogenic other Candida species. The pathogenic microorganism Candida albicans thus presents an example of from its own perspective exceedingly well accomplished parasitism.

Pleomorphism according to Enderlein is reflected in the example of Candida albicans also under modern, immunobiological perspectives. The levels of Pleomorphism in Candida albicans comprise the following:

- the pleomorphistic clinical manifestation of a Candidiasis
- the yeast mycelial dimorphism
- the generation cycle of Candida albicans with a basidiomycetic fungus
- the parasitic adaptation to the human host organism
- the actualization of the concepts according to Enderlein in the development of the SANUM preparations ALBICANSAN and EXMYKEHL.

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