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GENETIC DETERMINATION OF HOST-PARASITE RELATIONSHIPS IN MYCOTIC INFECTIONS*)

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Abstract. Results are presented of experimental work confirming the polyfactorial basis of virulence of the dermatophyte *Microsporum gypseum*, and the presence of genetic resistance to dermatophytosis in mice. Avirulent strains of *M. gypseum* may be altered to virulent strains by genetic complementation determined by the mechanism of heterokaryosis or diploid constitution. The complementation is interallelic in nature. The origin of clinical signs of mycotic infection depends on the interaction between the genome of the parasite and that of the host (mouse) at the gene level.

Nowadays, microbial infections are caused generally by microorganisms which are ubiquitous components of the environment, and persist in the body of the host without causing any damage if conditions are normal (Dubos 1967). It is of great importance to obtain knowledge of the conditions leading to the origin of pathogenicity of the microorganism. In mycoparasitology one can find a number of superficial and deep mycoses caused by fungi which, until recently, have been considered to be harmless saprophytes. The biological group of dermatophytes causing superficial mycoses of animal and man comprizes species which only seldom turn pathogenic, and occur mainly in the soil. These are intermittent species (between saprophytic and parasitic species) and, therefore, could serve as a suitable model for studies on the development of pathogenicity. Cultivation of these species is relatively easy, and their capability of reproducing sexually under conditions in vitro makes them suitable objects for experimental studies on the development and genetic basis of pathogenicity.

In this short communication, an attempt has been made to survey several results of our work. Within the last three years we have tried to answer four questions: 1. Is the virulence of the dermatophyte *Microsporum gypseum* controlled by mutable determinants? 2. What is the genetic basis of virulence? 3. Is alteration of virulent to avirulent strains, and vice versa, possible under experimental conditions? 4. Is the reaction of the host to mycotic infection under genetic control?

The polyfactorial basis of virulence has been confirmed for the dermatophyte *Microsporum gypseum* (Hejtmánek and Lenhart 1970a) by a crossing analysis. By means of UV-radiation we obtained avirulent mutants with two types of genetic markers, i.e., morphological and biochemical markers from a virulent strain. (Lenhart et al. 1972) The morphological markers under consideration were shape,

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pigmentation and sporulation of the colonies; the biochemical marker was auxotrophy with the inability of biotin- and inosite synthesis.

We observed that certain pairs of mutants growing together on the same medium showed spontaneous genetical complementation resulting in the origin of a prototrophic culture without nutritional requirements, and with a morphology identical to that of the wild strain (Lenhart 1972). This phenomenon is based on the fact that genetic information absent in one genome (mutant A) is completed by genetic information from the second genome (mutant B) after fusion of the cells in the common cytoplasm. This complementation is interallelic in nature. The two mechanisms responsible for its origin are heterokaryosis and diploid constitution. They can be differentiated experimentally, heterokaryons with the heterokaryon test, diploids by detection of mitotic recombinants, and by karyometry (Lenhart and Hejtmánková 1972). Under heterokaryotic conditions, the nuclei carrying marker genes retain their integrity and divide in the common cytoplasm without their direct interaction. The uninucleate spores differentiating during the growth of the culture, contain one or the other mutant genome, but never a complemented genome. After the spreading of the heterokaryotic spores, both components dissociate. In diploids, the two mutant nuclei fuse and form a diploid nucleus; thus, all uninucleate spores gain a stable, complemented genome. When the spores have spread, the components of the diploids do not segregate vegetatively.

Also the genes controlling the pathogenicity of the fungal parasite complement, and virulent strains originate from avirulent strains by genetic complementation (Hejtmánek and Lenhart 1972). The pathogenicity and the clinical picture of an infection caused by strains with complemented virulence is similar to that of wild strains.

In view of the fact that populations of these fungal organism sare heterogeneous in their natural biotopes, i.e., the soil, it appears that the mechanism of heterokaryosis and diploid constitution are active also under these conditions and, hence, responsible for the origin of virulent strains from avirulent strains. Contact with the viable host is not obligatory. The host serves only as a selective substrate for the virulent strains and their further distribution.

The finding that both virulent and avirulent strains were present in populations of geophilic dermatophytes (*M. gypseum*, *M. cookei*, *Trichophyton ajelloi*) supports our conclusion. The same applies to the fact that morphological mutants prepared in vitro in our laboratory, were isolated from the soil by American authors in Argentina (Hejtmánek 1972).

Our results indicate that the pathogenicity of the fungal parasite is determined by its genome. The avirulent mutant is constantly incapable of causing infection in the susceptible organism of the host and that neither with a high nor a repeated dose of inoculum.

Every infection, including mycoses, is the result of interaction between two living systems: the parasite and the host. Therefore, we started to investigate whether the defence reaction of the host to a known fungal parasite is under genetic control. We selected from a group of 33 different inbred strains of mice both resistant and susceptible strains to experimental infection with *Microsporum gypseum* (Hejtmánek 1970), and crossed them. The results of this crossing analysis of F_1 and F_2 and of the two back crossings indicated that resistance is determined by an autosomal dominant factor, susceptibility by recessive factor (Hejtmánek and Lenhart 1970b). Our results are consistent with the data on the incidence of dermatophytoses caused by different species of dermatophytes in populations of man of different races, and apparently controlled genetically as suggested by Vanbreuseghem (1967).

The results of our experiments in vitro and in vivo suggested that the origin of a mycotic infection with clinical manifestations is in mice determined by interaction between the genome of the parasitic fungus and the genome of the host. The mechanism of gene mutations and genetic complementation of virulence may lead to the preparation of strains with a graded virulence which may be utilized for preventive therapeutic purpose.

ГЕНЕТИЧЕСКАЯ ДЕТЕРМИНАЦИЯ ВЗАИМООТНОШЕНИЯ ХОЗЯИН-ПАРАЗИТ У МИКОТИЧЕСКИХ ЗАБОЛЕВАНИЙ

М. Гейтманек

Резюме. Автор подытоживает результаты экспериментальных работ, подтверждающих полифакториальную основу вирулентности у дерматофита *Microsporum gypseum* и наличие генетической устойчивости к дерматофитозу у мышей. Из авирулентных штаммов *M. gypseum* могут возникать вирулентные штаммы путем генетической комплементации. Эта комплементация проводится через механизм гетерокариоза или диплоидии и носит интералелический характер. Возникновение клинически проявленного микотического заболевания обусловлено уровнем генов путем интеракции генома паразита и генома хозяина (мыши).

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