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Review

Carotene derivatives in sexual communication of zygomycete fungi

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A B S T R A C T

Recognition between mating partners, early sexual morphogenesis and development are regulated by a family of β-carotene derived signal compounds, the trisporoids, in zygomycete fungi. Mating type-specific precursors are released from the hyphae and exert their physiological effects upon compatible mating partners. In a cooperative synthesis pathway, later intermediates and finally trisporic acid are formed. All trisporoids occur in a number of derivatives. Trisporic acid and some precursors directly influence the transcription of genes involved in sexual development. This has been demonstrated for *TSP*3, encoding the carotene oxygenase involved in sexually induced cleavage of β-carotene. Species specificity of mating despite a common and commonly recognized signaling system is maintained by several factors. Specific distribution and recognition patterns of the trisporoid derivatives and the proposed divergence in trisporoid synthesis pathways in diverse species play a role. The derivatives elicit vastly differing, partially mating type-specific responses during early sexual development. Another specificity factor is the realization of different regulation levels for the trisporoid synthesis enzymes in different species. Enzymes in the trisporoid synthesis pathway show remarkable variations in mating type-specific activity and the exact activation time during sexual development. This allows for the observed complex network of possible interactions, but at the same time forbids successful mating between dissimilar partners because the necessary transcripts or gene products are not available at the appropriate developmental stage.

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1. Aspects of mating reactions in zygomycete fungi

In zygomycetes, two facets of the mating reaction have been studied in greater detail: first, the sexual morphology as expressed by the emergence and development of specialized hyphae and other structures during the sexual life cycle, and second, communication physiology, dealing with the production of trisporoids, the chemical signals for partner recognition, and response to these same signals by the mating partner. Review articles focusing on these aspects of zygomycete mating have been published recently (Schimek and Wöstemeyer, 2006; Wöstemeyer and Schimek, 2007). The connections and interrelations between sexual development and its mediating signals are yet largely unknown. The present contribution deals especially with the regulation of sexual communication, its similarities and differences in various zygomycete species and the consequences thereof on mating specificity. A third aspect, the genetical base of sex, mating, and its

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regulation has hitherto not been in the focus of research for lack of data. With the identification of a sex-specific region in the *Phycomyces blakesleeanus* genome, research into the basis of sexual differences is finally possible. The sex loci unique for each mating type, sexM and sexP, both encode high mobility group (HMG) domain transcription factors (Idnurm et al., 2008) with yet unknown function. Studies on their expression and the range of their regulatory activities will provide new insights into the mechanisms of the mating process. Still, apart from the basic determination of mating type by these sex loci, the strict complementarity of the sexual communication system relying on the participation of both mating types in the production of the regulatory pheromones would be alone sufficient to govern the sexual differentiation programme.

The morphological features of sexual development are basically identical in all zygomycetes. The process culminates in the formation of a characteristic fusion zone between the two parent hyphae where the mature, name-giving zygospore develops (Fig. 1). It is contained within a thick-walled, often pigmented and ornamented structure, the zygosporangium. As zygomycetes are coenocytical fungi without regular septation, a large number of nuclei are finally incorporated into the zygospore. During zygospore maturation, the number of nuclei declines, and subsequently nuclear fusion and meiosis will take place. Heterothallic species comprise two mating types designated (+) and (−). When hyphae of the different mating types meet, a series of successive morphological changes takes place, bringing first the hyphal tips into close contact with each other and leading subsequently to the formation of swollen hyphal tips, gametangia, and finally the fusion zone. In homothallic species, these events will take place between branches of the same primary hypha. Best studied in its physiological aspects is the heterothallic development, namely in the three species *Blakeslea trispora* (Choanephoraceae), *P. blakesleeanus* (Phycomycetaceae) and *Mucor mucedo* (Mucoraceae). In all three species, distinct sexually committed hyphae, the zygophores, are formed, but only in *M. mucedo* they rise above the substrate mycelium and are therefore a good marker for sexual induction. *M. mucedo* reacts also most sensitively to stimulation with externally applied trisporoids (Sutter and Whitaker, 1981). Chemical recognition stands at the beginning of all sexual reactions and takes place both between the outermost hyphae in mycelial colonies approaching each other, and between the individual hyphae, may they be zygophores (Fig. 1) or hyphae branching out from the aerial mycelium in other species. Recognition of a suitable mating partner in turn stimulates the production of trisporoids in a feedback cycle (Wöstemeyer and Schimek, 2007). Asexual reproduction leads to the formation of sporangia at the tip of another type of aerial hyphae, the sporangiophores. Sexual development and asexual development are often separated spatially within the mycelium and in these areas are mutually exclusive in some species.

Trisporoids are a family of C_{18} or C_{19} isoprenoid compounds, all with a common C_{14} backbone structure (Fig. 2). The various intermediates formed in the trisporoid synthesis sequence are characterized by modifications of the residues at positions C(1) and C(4). The first observable trisporoid precursor after β-carotene cleavage is 4-dihydrotrisporin, which is later converted to trisporin and trisporol. In the (+) mating type, additionally 4-dihydromethyltrisporate and methyltrisporate are produced on the route to trisporic acid (Schimek and Wöstemeyer, 2006; Schachtschabel et al., 2008). Recent studies on trisporoid synthesis in *B. trispora* revealed that the physiologically highly active 4-dihydromethyltrisporate probably originates from another synthesis route and is apparently not a major intermediate for the production of trisporic acid. Instead, it gives rise to 4-dihydrotrisporic acid

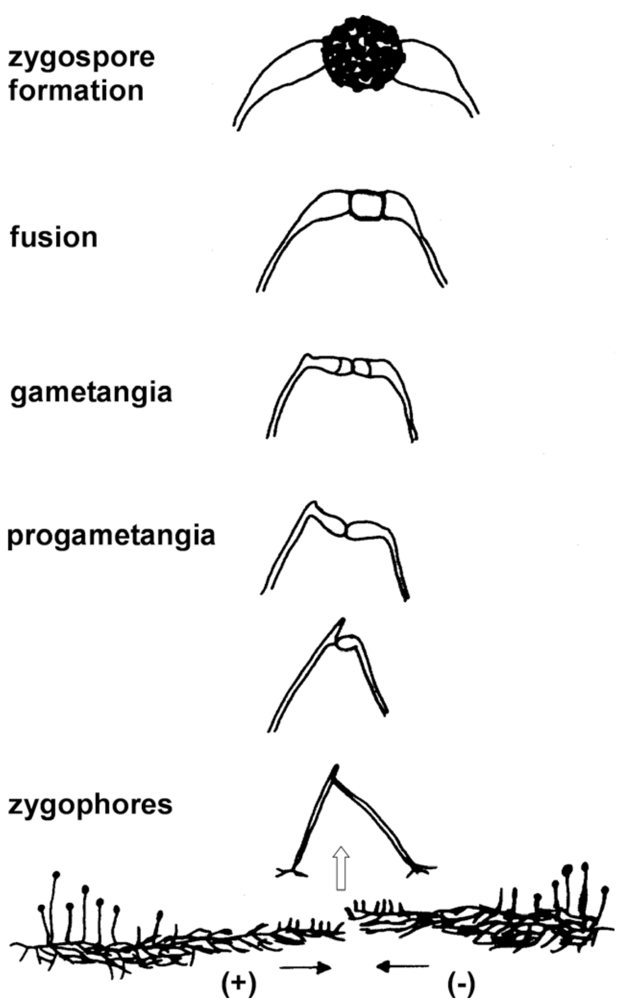
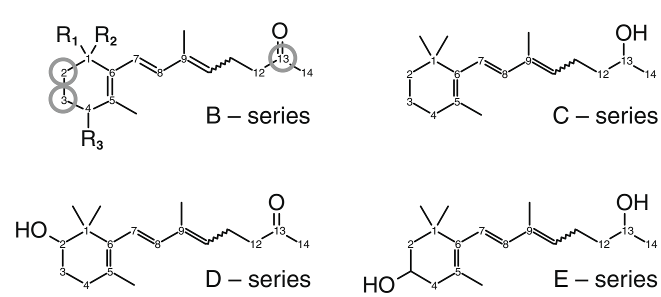


Fig. 1. Sexual development in *Mucor mucedo*. Zygophores develop from young mycelium when a mating partner approaches. Individual zygophores contact each other, only then further differentiation towards the formation of a zygosporangium is possible.



4-dihydrotrisporin: $R_1 = CH_3$; $R_2 = CH_3$; $R_3 = OH$
trisporin: $R_1 = CH_3$; $R_2 = CH_3$; $R_3 = O$
trisporol: $R_1 = CH_3$; $R_2 = CH_2OH$; $R_3 = O$
trisporic acid: $R_1 = CH_3$; $R_2 = COOH$; $R_3 = O$
4-dihydrotrisporic acid: $R_1 = CH_3$; $R_2 = COOH$; $R_3 = OH$
methyltrisporate: $R_1 = CH_3$; $R_2 = COOCH_3$; $R_3 = O$
4-dihydromethyltrisporate: $R_1 = CH_3$; $R_2 = COOCH_3$; $R_3 = OH$

Fig. 2. General structure of trisporoids. The diverse compounds are defined by modifications of the substituents at C(1) and C(4), the derivatives are characterized by the substituent pattern at C(2), C(3), and C(13). The physiologically occurring modifications of R_1–R_3 are shown only for the B-derivative, but may occur with all other derivatives, too. All listed trisporoids have been identified in culture extracts at least as B- and C-derivatives.