Redirection of pigment biosynthesis to isocoumarins in Fusarium

Colonies of Fusarium species often appear red due to production of pigments, such as aurofusarin or bikaverin. The primary compounds in these biosynthetic pathways are YWA1 and pre-bikaverin, respectively, catalyzed by two multidomain polyketide synthases (PKSs), which both have a claisen-type cyclase domain (CLC) in their N-terminal. Disruption of the CLC domains has been shown to result in formation of the lactones citreoisocoumarin and SMA93 instead of YWA1 and pre-bikaverin. In the present study we have discovered a medium with low nitrogen content which partially redirects the aurofusarin and bikaverin pathways to produce citreoisocoumarin and SMA93, respectively. This is the first time that SMA93 is identified in a fungus and we suggest that it is renamed bikisocoumarin, as it is derived from the bikaverin pathway. The redirection of the aurofusarin and bikaverin biosynthetic pathways was reverted by adding inorganic nitrogen to the medium, whereas organic nitrogen in form of arginine or glutamine stimulated isocoumarin production. This suggests that nitrogen source can influence isocoumarin production. Production of isocoumarin was also repressed by alkaline conditions, which suggests that nitrogen supply is not the sole regulatory factor in the pathway. The redirection was observed in all producers of aurofusarin (6) and bikaverin (2), suggesting the presence of a conserved regulatory mechanism.