Aspergillus, Penicillium, and Talaromyces are among the most chemically inventive of all fungi, producing a wide array of secondary metabolites (exometabolites). The three genera are holophyletic in a cladistic sense and polythetic classes in an anagenetic or functional sense, and contain 344, 354, and 88 species, respectively. New developments in classification, cladification, and nomenclature have meant that the species, series, and sections suggested are natural groups that share many extrolites, including exometabolites, exoproteins, exocarbohydrates, and exolipids in addition to morphological features. The number of exometabolites reported from these species is very large, and genome sequencing projects have shown that a large number of additional exometabolites may be expressed, given the right conditions ("cryptic" gene clusters for exometabolites). The exometabolites are biosynthesized via shikimic acid, tricarboxylic acid cycle members, nucleotides, carbohydrates or as polyketides, non-ribosomal peptides, terpenes, or mixtures of those. The gene clusters coding for these compounds contain genes for the biosynthetic building blocks, the linking of these building blocks, tailoring enzymes, resistance for own products, and exporters. Species within a series or section in Aspergillus, Penicillium, and Talaromyces have many exometabolites in common, seemingly acquired by cladogenesis, but some the gene clusters for autapomorphic exometabolites may have been acquired by horizontal gene transfer. Despite genome sequencing efforts, and the many breakthroughs these will give, it is obvious that epigenetic factors play a large role in evolution and function of chemodiversity, and better methods for characterizing the epigenome are needed. Most of the individual species of the three genera produce a consistent and characteristic profile of exometabolites, but growth medium variations, stimulation by exometabolites from other species, and variations in abiotic intrinsic and extrinsic environmental factors such as pH, temperature, redox potential, and water activity will add significantly to the number of biosynthetic families expressed in anyone species. An example of the shared exometabolites in a natural group such as Aspergillus section Circumdati series Circumdati is that most, but not all species produce penicillic acids, aspyrones, neoaspergillic acids, xanthomegnins, melleins, aspergamides, circumdatins, and ochratoxins, in different combinations.