The individual genetic susceptibility is a cornerstone in the pathogenesis of coronary artery disease (CAD). The search for the genetic background and the subsequently altered molecular mechanisms has been ineffective for several years. The increase in genome-wide association studies in recent years has changed the scenario and more than 40 variants have so far been identified to be highly significantly associated with CAD and the risk of myocardial infarction (MI). Whereas most of these findings affect frequent polymorphisms, exome-wide sequencing in families with a high prevalence of CAD revealed mutations with a high penetrance and as a consequence a high risk of suffering from MI. The findings allow a deeper insight into functional mechanisms involved in the pathogenesis of atherosclerosis. Furthermore, the data enables validation of the numerous epidemiologically identified risk markers with respect to the causal role in the development of CAD, making the genetic architecture of CAD much more transparent. Nevertheless, individual risk prediction has only made weak progress in the face of the new findings. Every individual without exception carries numerous risk alleles even when the number and effect strength shows individual differences. Thus, a varying degree of genetic susceptibility is shared by all of us. Current research is therefore focusing on the functional integration of genetic information to discover new approaches to prevention and therapy.