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Challenging GWAS discoveries by locus refining and stratification of population by anthropological lineages

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Genome Wide Association Studies (GWAS) are extraordinary opportunities to find culprit genes in complex conditions such as diabetes, obesity, metabolic syndrome (MetS) or polycystic ovarian syndrome (PCOS). Despite enormous progress (e.g. 831 MetS genes register in GAD) associated genes displayed relative low odds ratio and hardly explain heritability in populations. Although there may be multiple explanations, the European MEDIGENE program (FP7-279171) launched the hypothesis that dissecting anthropological lineages would be able to better stratify populations for GWAS. This is based on the ability to geo-localized individual DNA in Europe based on SNP (single nucleotide polymorphism), more or less concordant to mitochondrial (mt)DNA or Chr Y lineages. Focusing on Mediterranean populations, the project is studying native and immigrant populations (Albanians, Turkish, Maghrebin and Romanian) in Europe affected by MetS or PCOS. Among 30 prioritized genes screened by their leader SNP or proxies, we discovered in French and Romanians one of the most influential gene in PCOS acting as dual phosphatase. Other genes were more specific to male/female susceptibility for MetS. More than 4621 DNA samples with clinical and anthropological information were collected in the Mediterranean area or from more genetically-distant populations in Eastern Europe, Lithuania, Lebanon and Russia. We also obtained 400 samples of ancient (a) DNA from antique Romans from Tarragona Necropolis. While efforts are spent to detail haplotype structure with a customized Affymetrix chip, locus refining using Roche 454 technology is currently used for identification of rare SNP with major effect and that may be used to develop significant genetic markers at a clinical scale.

Biography

Florin Grigorescu graduated MD (Bucharest, Romania) and PhD (Montpellier, France) and completed his postdoctoral studies in Joslin Diabetes Center (Harvard Medical School, Boston). He is a senior investigator at INSERM (France), honorary professor in molecular genetics and member of national academy in Romania. He has published more than 100 papers in the field of insulin resistance and genetic syndromes and received the GB Morgagni (Italy) and French Academy (France) awards. He is actually the coordinator of the European MEDIGENE program (2012-2015) and leader of the Nutrition & Genomes team at the UPR-204 NUTRIPASS, Montpellier France.

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