

MEDIGENE PROGRAM REWARDED WITH THE EUROPEAN STARS AWARD 2017

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On December 4th 2017, the European program MEDIGENE (<http://cordis.europa.eu>) was awarded by the French Minister Miss Frédérique Vidal with the occasion of the 5th session of

“Etoiles de l’Europe” in the section Open Science (www.horizon2020.gouv.fr). The ceremony was carried out at the Musée du Quai Branly in Paris where the coordinator Prof. Florin Grigorescu, the manager of the program Christophe Normand, the team member Corinne Lautier and the president of SME INTACTILE Design Yves Rinato received the price. The decision was taken by an independent jury presided by Prof. Jean Chambaz from the University Pierre and Marie Curie in Paris. The award recompenses the coordination from France of European programs. In face of ambitious goals of MEDIGENE, we express our gratitude for this distinction in the context of numerous participants in the Mediterranean countries.

MEDIGENE program was proposed in the Seventh Framework Program (FP7) to understand genetic and environmental factors in pathogenesis of insulin resistance of ethnic populations in the Mediterranean area. Although linked with practical purposes in clinical genetics, endocrinology and metabolism (more than 6050 DNA samples were obtained), the program is original trying to marriage various fields in science, including clinical genetics, anthropology and even archaeology comprising a consortium of 20 countries (<http://www.umontpellier.fr/articles/prix-distinctions>). The working hypothesis was far from trivial since the coordinating team proposed to investigate by genetic markers usually used in GWAS - called SNP – several gene candidates for metabolic syndrome at a much higher genome density. Moreover, the project proposed to make the correlation with well-known uniparental markers on Chromosome Y or mitochondrial (mt)DNA usually used in anthropology.

While the major goal remain challenging, coordinating team at the University of Montpellier, France acknowledge efforts made by all participants in recruiting patients under special conditions combining anthropological, metabolic and genetic contexts. The “C.I. Parhon” National Institute of Endocrinology in Bucharest and Faculty members at “Carol Davila” University in Bucharest had a major contribution.

Romania, by its representative Prof. Mihail Coculescu - passed away in March 2016 - and then by Professors Catalina Poiana and Corin Badiu who continued his work, had a major contribution. This was felt from the beginning by profound understanding of the original aspect of the program and then, by the actual contribution during 5 years. Indeed, one major contribution of Romanian scientists was the understanding of primary goal in recruiting subjects from well-defined geographic regions of Romania (e.g. Prof. Carmen Georgescu in Cluj, Transilvania and Monica Gheorghiu, Serban Radian in Bucharest at “C.I. Parhon” Institute). These so called anthropological samples, although unusual in clinics, were of high value allowing the charting of DNA in Europe and comparison with other more genetically distant populations (e.g. populations studied by Elza Khusnutdinova and Serghey Litvinov in Russia or Yildiz Tutuncu and Ilhan Satman in Turkey). Many of you asked probably why Romania was included in such a project of Mediterranean populations? Because Romania, called in antique times Dacia - received during the Roman Empire for a part of its population at the south of Danube – the name of Dacia Mediterranea, where Dacian population was deported by romans. This event might be insignificant in the context of population admixture for millennia or studying actual health problems, but has the merit to raise the consciousness on the diversity of European populations, the link with history and how we can define ethnic populations in a country in a manner that medical doctors in genetics understand genetic variability in Europe. This was not the only reason. Romania was included because – albeit not expressly recognized – scientists

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were aware that the gradient of genetic susceptibility in Europe for insulin resistance concerns both East – West and North - South axis. This explained why some samples were required from Romania, including Moldovans and northern Lithuania (Prof. Valentinas Matulevicius) or far Northern Siberia in Russian Federation. Undoubtedly, multiple sampling considerably complicated the program since in genetic anthropology investigators need a powered number of samples (minimum of 50 samples per group) to draw significant conclusions from genetic markers. Therefore, these investigations should be continued to complete DNA sampling in a way to render our genetic database (MAGDB) at a high standard in European research. Fortunately, talented work of Russian partners allowed us to draw conclusions in MEDIGENE on diversity of populations that can be included in GWAS – mainly Albanian immigrants from Italy and Greece - compared to native Albanians (Dorina Ylli and Prof Agron Illy from Tirana), Romanians in Spain (Felicia Hanzu, Laura Brugnara and Prof Ramon Gomis) and Turkish in France (Prof Michel Pugeat from Lyon France). Last but not least, Romania also contributed with new hypothesis in investigation of metabolic syndrome among which the most important were the involvement of arginine-vasopressin (AVP) pathway in arterial hypertension (thesis of Madalina Vintila) and the role of genes from the androgen pathway in polycystic ovary syndrome (work in WP8 of Nicoleta Baculescu in collaboration with Michel Pugeat in France). These last results were unexpected, very original, which will have a major impact in understanding pathogenesis of metabolic syndrome.

We would like also to acknowledge the contribution of Romanian practitioners in providing nutritional data, collected through MEDIPAD device created by nutritionists in partnership with Intactile Design SA (<http://intactile.com>). Nutritional data (Prof Dan Chetea) were of extreme importance as indicated by excellent progress in nutrigenomics made in collaboration with the French group. Initially, nutritional data were supposed to help understanding of insulin resistance in terms of energy consumption. It turned out that results largely overpassed this aspect raising new issues on the role of branched chain amino-acids (BCAA) or genes in the FGF21 pathway and allowing the implementation of a new database of BCAA (thesis of Sara Haydar in Montpellier).

We cannot conclude on the outcomes of MEDIGENE program without acknowledging the efforts of the University of Montpellier by its informatics department (DSI) implementing the MEDIGENE server in connection with all Mediterranean countries ([\[www.languedoc-roussillon.inserm.fr/actualites\]\(http://www.languedoc-roussillon.inserm.fr/actualites\)\). This structure is now functional and supposed to be used in future European programs. Secure data is an obligatory condition for developing genetic databases under actual European ethical regulations. We hope that all conditions created through MEDIGENE funding from EC represent a starting point of numerous other collaborations between European countries. Widening knowledge in Europe and strengthening defined field of research in universities represent new goals to be attained in the near future \(<https://occitanie-europe.eu/5e-edition-des-etoiles-de-leurope-un-prix-pour-lengagement-europeen-des-chercheurs-en-france/>\). New projects should be proposed to stimulate excellence and innovation capacities of research groups from Romania and other East countries.](http://</p>
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There are many aspects approached in the MEDIGENE program for which the reader is invited to consult the final report (<http://cordis.europa.eu/docs/results/279/279171/final1-final-report-v7.pdf>). There is however one aspect that merits to be underlined with the occasion of reconnaissance from officials. Molecular genetics will cover in the near future the majority of preoccupations in clinics and endocrinology. France is ready to cooperate with other European countries in achieving a high level of technology. This is even one major mission of the NUTRIPASS group (UMR204 IRD, Univ. Montpellier, SuprAgro) in France (<http://www.nutripass.ird.fr>). However, all these progresses will rapidly become insufficient whether representatives of institutions do not understand that diversity of populations and complexity of genetics mechanisms is the real challenge for the future diagnosis of non-Mendelian complex disorders. Therefore, in parallel with technological developments, institutions should take decisions in allowing multidisciplinary investigations combining genetic anthropology, ecology and clinical medicine (<http://www.umontpellier.fr/recherche>). In this direction, the collaboration with groups in anthropology (e.g. Institute of Anthropology in Zagreb – Sasa Missoni) appears essential and investigators in MEDIGENE should be aware of dramatic changes that we expect in future years in Europe and world wild. In 2050 there will be 9 billions of individuals among which more than 25% will display “diabesity” that will cover almost 15% of health expenses. There will be also major migration fluxes from South to North and dramatic dropping in the fertility rate. MEDIGENE program had the quality drive the attention towards these aspects of future research and participants should be proud to have the courage the launch new hypothesis in research that will help the evaluation of genetic risk for chronic diseases.