

€UROPEAN FUNDING FOR REPRODUCTION RESEARCH— A MULTINATIONAL PERSPECTIVE

Funds from the European Union are not the only source available to the continent's reproductive research community. Each country independently sponsors the work of these scientists, but, as illustrated by snapshots in the following pages, there are huge differences in the commitment of the various European nations to tackle the challenges of reproductive biomedicine.

Spain

Carlos Simón

Research in reproductive biology in Spain has increased in the past decade in accordance with the clinical impact of the field, as measured by the number of *in vitro* fertilization (IVF) clinics and IVF cycles performed in the country. The Spanish Fertility Society Registry reports that in 2004, a total of 38,886 IVF procedures in 116 IVF centers were performed, corresponding to 10% of the total number of cycles reported in Europe.

Neither the Spanish Ministries of Health and of Science and Innovation nor the local governments earmark specific funding for reproductive biology. Nevertheless, the cost of the research projects in reproductive biology currently funded by the Ministry of Science and Innovation in 2006–2007 is ~€2.5 million, funds for approximately 20 projects every year.

Private funding, in turn, comes largely from Merck-Serono and Schering-Plough, which every year provide €20,000 for one two-year project through the Fundación Salud 2000 and €30,000 for an international award, respectively.

Lastly, reproductive biology is represented in Spain by three national societies—Sociedad Española de Fertilidad (SEF), Asociación Española de la Biología de la Reproducción and Sociedad Española de Reproducción Animal—but their financial input is small. SEF provides ~€12,000 per year for research funding.

A search of the Spanish papers published between 2004 and 2008 in the 25 journals indexed in the ISI Web of Knowledge within the category 'Reproductive Biology' discloses 823 publications (~164 peer-reviewed papers per year). Basic research comes from universities and academic institutions, whereas most clinical investigation originates in IVF clinics. Translational research, which requires both basic and clinical expertise, is being done through foundations set up by the most important reproductive centers. In this regard, the Instituto Valenciano de Infertilidad Foundation, which has invested €500,000 per year in research, is worthy of mention, as it has produced approximately 20% of the 823 papers mentioned above.

The prospects of research on reproductive biology in Spain look promising. Teaching initiatives are flourishing, and Spain offers six master's programs in reproductive biology in different regions of the country. In addition, Spanish law has taken one of the most liberal stances in Europe, allowing for research involving human embryos. These circumstances, plus the volume and impact of Spanish research in reproduction, allows one to be optimistic about the future of this discipline in our country.

Carlos Simón is at Instituto Valenciano de Infertilidad, University of Valencia, Valencia, Spain.
e-mail: csimon@ivi.es

Belgium

Thomas M D'Hooghe

Women's health, including reproductive biology and medicine, is not a research priority on the Belgian agenda, in contrast with health issues such as cancer and in contrast with the US situation, in which a specific US National Institutes of Health branch—the National Institute of Child Health and Development—attends to this topic. This situation is at odds with the fact that infertility affects one in eight couples globally and the recognition that assisted reproductive technologies are a key part of national strategies addressing demographic and reproductive challenges.

Belgian researchers applying for European research funding in reproductive biology are faced with the fact that neither the EU FP6 nor the EU FP7 health research program included a specific call for research projects in their field, making it necessary for them to apply for more highly competitive research categories. Our group, for example, is a partner in the European Network for Endometriosis, supported by the first-ever endometriosis grant provided by the EU Public Health Work Plan in 2006.

Individual research groups can apply for investigator-initiated grants to pharmaceutical companies, but research topics likely to be funded are often limited to the primary interests of these companies. I hold the Merck Serono Chair of Reproductive Medicine at Leuven University (2005–2010) and have received yearly funding (€60,000 per year) from Merck Serono Belgium to do research without any involvement of the company. But this situation is the exception rather than the rule.

Within Belgium, Flanders has recently increased its investment in research and development, but, again, reproductive biology is not a clearly labeled research priority. Moreover, reproductive biology funding from charities is also absent. So, as in the case of European grants, researchers in reproductive biology need to apply in more general categories for research funding (€300,000–500,000 for a four-year research grant and €150,000 over four years as salary stipend for a PhD student) to the

two main public funding agencies in Belgium—the Fund for Scientific Research (FWO) and the Institute for Science and Technology.

Even if one is lucky enough to secure national funds, continuity may be a problem. For example, for the past 10 years I have received a FWO grant as principle clinical investigator (€50,000 per year) that has allowed me to devote 50% of my time to research in endometriosis, half-time away from the clinic. However, at the end of the grant period, I may have to go back to clinical medicine full time at the expense of the 12 PhD students working under my supervision.

Finally, in Leuven University and its affiliated hospitals, it is possible for clinical investigators to apply for a variety of grants and awards (four-year research grant for established scientists ranging between €200,000 and €600,000), but the competition is increasingly tough for translational research. And the Flemish Institute for Biotechnology, an excellent but highly selective interuniversity research platform, does not have a research line in reproductive biology and medicine.

In my view, the only way that reproductive medicine and biology can be identified as a high-priority research area on a university level is by creating a large research group on the basis of increased internal collaboration among smaller groups as well as with strong groups in the areas of human genetics, transgenesis and systems biology techniques. Furthermore, active lobbying is needed to give higher priority to women's health and reproductive biology at both the national and European levels.

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Thomas M. D'Hooghe is at Leuven University Fertility Center, Leuven University, Leuven, Belgium.
e-mail: thomas.dhooghe@uz.kuleuven.ac.be

Croatia

Daniel Rukavina

Although Croatia is already in an advanced phase of negotiations regarding its incorporation into the EU, it is going through the difficulties that all other transition countries have experienced (such as institutional development, research careers, funding instruments and underfunding of science and higher education), with the added complication of having lived through the recent war. All of these difficulties have impinged upon the allocation of funds for Croatian science, which are substantially lower than the objective set by the EU for its member states.

Funds for science from the private sector in Croatia are negligible. Thus, the whole burden falls upon the national budget. Fortunately, government investment in scientific infrastructure at universities and scientific institutes has increased considerably during the past few years. Coupled with increased employment opportunities for scientists and with the success of the Return of the Croatian Scientists from the Diaspora Program of the Croatian Ministry of Science, Education and Sports (MSES), there are reasons to be optimistic.

Even though Croatia has a negative population growth rate, it has neither a relevant and active reproductive health advancement policy nor a program for research in the field of human reproduction. The financial support from the MSES is the only aid for research in the field of human reproduction. Currently, there are 22 projects in human reproduction that are fully or partially subsidized with modest

amounts of money (~€250,000), which represent 1.24% of the total resources that the MSES allocates for projects in all scientific fields. In the framework of this program, of which I am one of several coordinators, the Ministry also provides salaries for 31 PhD students and some funds for equipment. In 2007, this support was ~€800,000, distributed among 22 research projects that focused on male and female infertility, reproductive pathology and animal reproduction.

Because the national funds for reproductive research are not sufficient, researchers in the field have developed collaborations with numerous research groups in Europe, the US and Japan. We also apply for international funds that increase the resources for research materials and ensure specialization scholarships for scientists in training. For example, together with colleagues from other EU countries I have applied for money from the FP6 in the framework of the European Network of Excellence for research on the mechanisms of embryo implantation control.

In my experience, the combination of national and international sources of funding and networking with Centers of Excellence within the European region are of the greatest importance for the fast development of science in countries in transition and for bridging the gap with more developed nations.

*Daniel Rukavina is at the University of Rijeka, Rijeka, Croatia.
e-mail: daniel@medri.hr*

Greece

Antonis Makrigiannakis

The EU parliament recently acknowledged that infertility is one of the causes of demographic decline throughout Europe. Greece has faced serious demographic changes during the past two decades owing to declining birth rates. Therefore, one would expect adequate funding for research in this field from the Greek Ministries of Health or of Education. Alas, reproductive biology research is poorly funded in Greece, far from European and US standards in terms of both private and public funding.

When I returned to Crete in 2002 after working for four years in the US and UK, my experience was rather disappointing. I founded the Laboratory of Human Reproduction in the Department of Obstetrics and Gynecology at the University of Crete and recruited PhD students and technicians with great difficulty. I quickly realized that I had to apply to different organizations to obtain sufficient funding for my research and received funding mainly from two sources: the Alexandros Onassis Public Benefit Foundation and the General Secretariat for Research and Technology of the Greek Ministry of Development (total €140,000). In addition, I received a small research grant from a pharmaceutical company for research in the field of obstetrics and gynecology and a grant from the Greek State Scholarship Foundation for collaborative basic research between Greece and another European country (in my case, Germany; total €45,000). Also, one of my PhD students received a philanthropic

private funding stipend (€18,000). Remarkably, none of this funding was specific for research in reproductive biology.

The support from the Alexander Onassis Public Benefit Foundation deserves mention: although its program is not intended to support particular reproductive biology research, it gave me a two-year grant for training in the US and then a grant to start my own projects in Greece, allowing me to perform basic research that would not be possible otherwise. Of note, the General Secretariat for Research and Technology of the Ministry of Development does not announce the specific fields that it plans to support. Instead, it expects investigators to come up with research projects, letting all branches of science to compete with one another during the application process.

The funding situation in Greece indicates that the problems related to infertility are unrecognized by policy makers. The administrative burden required for applying for a European research contract through Framework Programs is enormous, and the necessary core facilities are hard to obtain. My laboratory is one of the very few places in Greece conducting basic research in reproductive biology, and even if the funding opportunities are extremely limited, I expect our research to prosper in the years to come, building on the success of our scientific program on the immunotolerance of the fetus during implantation.

*Antonis Makrigiannakis is at the University of Crete, Crete, Greece.
e-mail: makrigia@med.uoc.gr*

United Kingdom

Hilary Critchley & Philippa Saunders

Sponsors of reproductive research in the UK include the government—the support of which is administered through the Medical Research Council (MRC), the Chief Scientist Office (Scotland) and the Biotechnology and Biological Sciences Research Council—as well as funds from many medical research charities including the Wellcome Trust, Wellbeing of Women (WoW) and Tommy's the Baby Charity. All of these organizations recognize that sexual and reproductive diseases are common and that new research is needed to develop new approaches to treating them.

In the 2007 UK Clinical Research Collaboration Association of Medical Research Charities report, an analysis of research funded by medical research charities during 2004–2005 (a combined amount of £63.7 million) showed that the proportion of funds spent in reproductive health was only 1.6% of the total. By comparison, data from the Scottish Executive Health Department indicates that the proportion spent by the Chief Scientist Office on Reproductive Health during the same period was 5–10% of the total.

The MRC is a major supporter of reproductive research—in 2007–2008 it committed ~£9 million to studies in reproductive, fetal and pediatric health. This amount includes strategic investment in the form of core funding (£22.5 million for the 2006–2011 period) for the MRC Human Reproductive Sciences Unit located in the Centre for Reproductive Biology at the University of Edinburgh. This center, formed in 1972, also houses the University Division of Reproductive and Developmental Sciences, which receives MRC funding of ~£1 million per year. Research within the Centre receives funds from charities as well, including Piggy Bank Kids (£1.6 million during 2004–2010).

Tommy's the Baby Charity funds work on pregnancy-related diseases. In 2007–2008, this charity gave £1.35 million for research and provided core support to the Maternal and Fetal Research Units at St. Thomas's Hospital in London and at St. Mary's Hospital at the University of Manchester. In 2008, a third center with funds from the same charity opened at the Centre for Reproductive Biology in Edinburgh to study the impact of maternal obesity during pregnancy.

The Wellcome Trust supports basic and clinical research in reproductive biology. Its 2006–2007 budget included two program grants awarded to Imperial College London and to the University of Birmingham for research on reproductive endocrinology and metabolism. Also, WoW's 2007–2008 budget of £2.02 million funded the areas of pregnancy and childbirth (72%), gynecology (15%) and quality of life (13%). Lastly, studies related to the impact of environmental factors on fetal development and lifelong health have been supported by funding from the EU to consortia with members in centers in Aberdeen, London and Edinburgh.

In conclusion, the UK research environment is becoming more challenging, as funding bodies place an increasing emphasis on translating laboratory work into patient benefit. Despite this fact, funding agencies remain committed to supporting reproductive research.

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Hilary Critchley is at the University of Edinburgh and Philippa Saunders is at the MRC Human Reproductive Sciences Unit, Edinburgh, Scotland.

e-mail: hilary.critchley@ed.ac.uk and p.saunders@hrsu.mrc.ac.uk

Germany

Thomas Strowitzki

In recent years, reproductive biology and medicine have not been the main focus of research funding in Germany. Research on human embryos is strictly forbidden according to the German Embryo Protection Law, but there is excellent reproductive research in animal models. This quality has been recognized by the German Research Foundation—the Deutsche Forschungsgemeinschaft (DFG)—and several projects in these models have therefore been funded in the past few years.

A three-year project coordinated in Essen to study epigenetic aspects of assisted reproduction was awarded ~€1.3 million in 2006. In Giessen, there is a Clinical Research Unit on male factor infertility resulting from impaired spermatogenesis, which has €1.1 million in funds. Smaller projects in reproductive biology are funded by individual grants from the DFG, such as a research program on mechanisms of embryo-maternal communication based in Munich, and some universities provide support in local scientific priority programs.

However, the most important contribution to research in reproductive biology in Germany by far is the new research group on 'the germ cell potential', coordinated in Münster. Ten projects from closely linked groups based all over Germany have a total of €3.4 million for the next three years to study, among other topics, *in vitro* maturation of gametes.

Aside from public funding, there are no private foundations with a focus on reproduction. This might be a reflection of the importance that research in reproductive bio medicine has in Germany's public opinion.

Finally, in terms of international funds, some German groups are part of the European Network of Excellence on Embryo Implantation Control, supported by the 6th Framework Programme of the European Commission.

In times of increasing infertility problems, the growing importance of reproductive medicine in Germany has been acknowledged, as far as clinical assisted reproductive techniques are concerned. A recent demographic study of the Berlin Institute for Population and Development underlined the strong acceptance of infertility treatment in German society and gained a high grade of public interest. However, more public support for research to optimize medical treatment is imperative. For example, aside from individual grants for university research groups, Germany's Federal Ministry for Education and Research has no nationwide framework program or initiative specifically dedicated to reproductive biology. Strategic support of this kind is urgently needed.

Thomas Strowitzki is at Ruprecht Karls University, Heidelberg, Germany.

e-mail: thomas.strowitzki@med.uni-heidelberg.de