[November, 08 - 16:45 - Room A]

OC - Research in Protozoology: Basic, Strategic, Applied or Operational?

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"Science: The Endless Frontier" was the name chosen by Vannevar Bush, advisor to the President of the United States, for the report he issued after World War II on the role science should play in the post-war period[1]. This report proposed the linear model' of technological development that shaped the policy of the USA and several countries:

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Basic research $\longrightarrow$ Applied research $\longrightarrow$ Technological development $\longrightarrow$ Manufacturing and operations

Basic research, according to Bush's vision, was carried out without possible applications in mind and represented the pacemaker and the remote dynamo of technological progress. In his linear model there is a tension between *understanding* (basic research) and *use* (applied research), activities that were to be kept apart and carried out by different people, institutions and organizations.

The launching of the Sputnik by the former Soviet Union in 1957 and the technological successes of countries that did not have a tradition in basic research [1] were key events challenging the linear model and stimulating further studies on how knowledge is produced and translated into use in contemporary societies. Gibbons and collaborators proposed that knowledge can be produced in two different ways[2]: The traditional form, where problems are set and solved in a context governed by the, largely academic, interests of a specific community (Mode 1) and a new form, where knowledge production is carried out in a context of application (Mode 2). Mode 1 is disciplinary, characterized by homogeneity, is hierarchical and tends to preserve its form; Mode 2 is transdisciplinary, characterized by heterogeneity, more heterarchical and transient. Quality control in Mode 1 is determined essentially through peer review judgments about the contributions made by individuals; In Mode 2 additional criteria are added through the context of application, incorporating social, economic and political interests (e.g. *'will the new drug be cost-effective? will it be socially acceptable?'*)

In parallel to the diversification of ways to produce new knowledge, the biological and biomedical sciences experienced profound transformations. The advent of genomic sciences made discovery research' as relevant as the traditional hypothesis-driven research'[3]; The era of Molecular Biology (study of complex phenomena by analysis of its molecular components), now sees the dawn of Systems Biology that goes in the opposite direction, reconstituting complex systems from individual components[4].

The field of Protozoology can be particularly sensitive to these transformations:

– Many killer diseases affecting poor and marginalized populations such as malaria, leishmaniasis, Chagas disease and sleeping sickness are caused by protozoal pathogens and therefore researchers will need to deal with funding agencies, international R&D programs, public health systems and industry operating in Mode 2' of knowledge production - and it is known that universities are not ready [2] for this ;

– The genomes of these pathogens and their insect vectors are being sequenced [3], opening new challenges and opportunities for scientific research, product development and public health[5].

Brazilian policy on science, technology and innovation has historically operated in Mode 1 and therefore quite disconnected from industry and public health needs and goals. Researchers working in Protozoology, however, can look at these issues through an optimism lens':

– The origins of Brazilian biomedical sciences have been traced to the pioneering public health work of Oswaldo Cruz, to the discovery of American trypanosomiasis by Carlos Chagas in 1909, and to the synergistic way they conducted basic and applied research[6-8];

– Several Brazilian protozoologists are already used to work in Mode 2, funded by national and international health R&D programs adopting quality control based on scientific merit and public health relevance. . Their labs are familiar with the so-called use-inspired basic research' of Pasteur's Quadrant[9];

– Success stories in microbial genomics in Brazil [4] demonstrate the existence of an enabling environment capable of actively exploring the promises of genomics/ proteomics sciences.

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[1] Frequently cited are the examples of the photographic and automobile industry of Japan, challenging the Germany and US competitors, respectively.

[2] See for instance http://www.davidsteven.com/Knowledge/seminar1intro.html

[3] See articles published in Nature, 3 October 2002 on the genome of *Plasmodium falciparum and in Science*, 4 October 2002 for the genome of *Anopheles gambiae*

[4] Brazilian labs have already sequenced e.g. the genomes of *Xylella fastidiosa, Chromobacterium violaceum and Leptospira interrogans*

[November, 10 - 21:00 -]

CC - Use of stem cells in the experimental and human chagasic cardiopathy

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A progressive destruction of the myocardium occurs in about 30% of *Trypanosoma cruzi*-infected individuals, causing chronic chagasic cardiomyopathy, a disease so far without effective treatment. Syngeneic bone marrow cell transplantation has been shown to cause repair and improvement of heart function in a number of studies in patients and animal models of ischemic cardiopathy. The effects of bone marrow transplant in a mouse model of chronic chagasic cardiomyopathy, in the presence of the disease causal agent, i.e., the *T. cruzi*, are described herein. Bone marrow cells injected intravenously into chronic chagasic mice migrated to the heart and caused a significant reduction in the inflammatory infiltrates and in the interstitial fibrosis characteristics of chronic chagasic cardiomyopathy. The beneficial effects were observed up to six months after bone marrow cell transplantation. A massive apoptosis of myocardial inflammatory cells was observed after the therapy with bone marrow cells. Transplanted bone marrow cells obtained from chagasic mice and from normal mice had similar effects in terms of mediating chagasic heart repair. The mechanisms of myocardial repair may include stem cell fusion and transdifferentiation into cardiomyocytes. These results showed that bone marrow cell transplantation is effective for treatment of chronic chagasic myocarditis and indicated that autologous bone marrow transplant may be used as an efficient therapy for patients with chronic chagasic cardiomyopathy. In order to test the efficacy of bone marrow cell transplantation in humans, a phase I trial was initiated. Patients with heart failure due to Chagas' disease, NYHA functional classes III and IV despite the optimized clinical therapy, were selected. An infusion of autologous bone marrow mononuclear cells was slowly injected into the three coronary arteries. The following measurements were assessed before, 1, 2, 4 and 6 months after transplantation: ejection fraction; left ventricular end diastolic diameter; serum Sodium levels; Minnesota living with heart failure questionnaire score; and distance walked in the 6-minute walking test. Twenty-two patients were treated so far. The analysis of 10 patients with 6 months of segment demonstrated a significant improvement in all the parameters listed above. These results show that intracoronary injection of bone marrow cells may be performed, suggesting that this is a safe procedure in patients with Chagas' disease heart failure. Our preliminary data also indicate that this therapy is potentially effective. Financial support: IMBT/MCT, FIOCRUZ, CNPq, FAPESB, NIH ricardoribeiro@cpqgm.fiocruz.br