Rockefeller Foundation: Biomedical and Life Sciences Offshoots

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Introductory article

Article Contents

Online posting date: 15th December 2010

Established in 1913 in New York City, United States, the Rockefeller Foundation (RF) was the most influential philanthropic foundation sponsoring the biomedical and life sciences in the first half of the twentieth century. It emerged as a key policy maker in steering the course of biological progress as part of a global strategy to promote social stability. The RF also pioneered interdisciplinary activities, most notably the transfer of technologies from the exact sciences to biology, which played a role in the rise of molecular biology. The molecular revolution in biology and medicine, which reached a peak in the 1960s and is still unfolding, can be traced to the technocratic, international and interdisciplinary policies pursued by the RF in its interwar heydays. After Second World War, with the advent of massive governmental support for science, the RF phased out its programs in science and medicine, focusing instead on promoting the 'Green Revolution' in Third World agriculture.

Introduction: Biological Progress as the Key to Social Stability

The Rockefeller Foundation (RF) was the most influential philanthropic foundation sponsoring the biomedical and life sciences in the first half of the twentieth century. Its influence peaked in the interwar period when governmental support of biological and biomedical research remained modest, especially in the United States and France. Before the establishment of RF in 1913, the major philanthropic activity of the Rockefellers in the biomedical area pertained to the creation, in 1901, of the Rockefeller Institute for Medical Research in New York City, modelled after the Pasteur Institute (Stapleton, 2004). During, and after, First World War, RF's main activities were in the public health arena, concerning especially the eradication of hookworm disease in the southern United States and malaria in southern Europe (Murard and Zylberman, 2000; Picard, 1999; Schneider, 2002; Stapleton, 2000; Weindling, 1997). **See also**: History of Hookworm; History of Malaria; Institut Pasteur and Satellite Institutes; Malaria

During the 1920s, RF's policy of 'making the peaks higher' favoured the, then revolutionary, physical sciences. A special relationship between RF and the life sciences began in the early 1930s, with the completion of an internal reorganisation between 1928 and 1932. A major outcome of that process was not only a new structure of Divisions each dealing with a major area of scientific knowledge, that is, the natural, medical, social and human sciences, but also a new, more interventionist policy. That policy, ratified in 1933, at a time when the Great Depression and the rise of Fascism threatened the progressive social order of liberal democracies, emphasised both a greater accountability for funds and a new goal of steering scientific progress in the direction of social stability, or away from 'social unrest' (Abir-Am, 1982, 1995, 2001, 2010); Abir-Am *et al*., 1984; Fisher, 1978; Kohler, 1991; Kay, 1993; Picard, 1999; Gemelli, 2000; Schneider, 2002).

The reorganisation of the Rockefeller Philanthropic Boards into the RF in the period 1928–1932 preserved the traditional interest of the founders, the entrepreneur John D Rockefeller Sr. and his heir, John D Rockefeller Jr., in medically related charities. But it also expanded that interest into a comprehensive promotion of scientific progress, or a progress believed to be necessary for securing social stability in an era of great social, economic and political turmoil. Coordination of RF's several Divisions was provided by the interdisciplinary orientation of its officers, as well as by administrative forums, such as the officers' conference, which ensured that projects presented for Trustee approval would reflect some measure of coherence. For example, boundary topics between the Natural and Medical Sciences Divisions were routinely discussed among their officers and especially their Directors, the veteran and influential Alan Gregg of the Medical Sciences Division (with the Division since 1922

ELS subject area: Science and Society

How to cite:
Abir-Am, Pnina G (December 2010) Rockefeller Foundation: Biomedical and Life Sciences Offshoots. In: Encyclopedia of Life Sciences (ELS). John Wiley & Sons, Ltd: Chichester.
DOI: 10.1002/9780470015902.a0003413.pub2

and as Director from 1930 to 1951) and the hardworking Director of the Natural Sciences Division who held office from 1932 to 1953, Warren Weaver. Both Gregg and Weaver became vice-presidents in 1951 and 1953, respectively (Schneider, 2003).

RF's new emphasis upon the life and biomedical sciences was influenced by the prevailing rhetoric on biological progress as a guarantor of social progress or of biology as the science of life. The social promise of biology was further contrasted with the physical sciences, which were persuasively portrayed as the sciences of death in the decade following their use in First World War carnage. Leading spokesmen of the scientific community, most notably the Nobel Laureate biochemist and President of the Royal Society of London, Sir Frederick Gowland Hopkins, articulated this point at the Centennial Meeting for the British Association for the Advancement of Science. Held in London in 1931, this was one of the best attended international scientific gatherings. Hopkins' address enjoyed substantial coverage, thus reaching and influencing RF's new Director of the Natural Sciences Division, Warren Weaver, who persisted in that position for two decades. An engineer, and protégé of RF President during the reorganisation and until 1936, Max Mason, Weaver chose to emphasise not biology itself but those aspects of it that were most amenable to the transfer of technologies from the exact sciences. This emphasis played a role in the rise of molecular biology to hegemony in the scientific imagination by the end of the twentieth century. **See also**: History of Molecular Biology; Hopkins, Frederick Gowland

Organisation: International and Interdisciplinary Features of RF's 'Program and Policy'

In addition to its interdisciplinary emphasis, RF's policy towards the biomedical and life sciences was also farsighted in retaining an international scope. That scope began with emergency public health measures in the aftermath of First World War, when RF led public health campaigns for the eradication of contagious diseases in France, Italy and other European countries, while increasing its presence in the life sciences into the 1950s. RF's active involvement in the support of European science, which included the rescue of some grantees before and during Second World War, persisted despite the isolationism of US governments in the interwar period. Although RF's investments in European science were only a quarter of those in American science, its extensive coverage of Europe, from Spain in the southwest to Sweden in the northeast, had created a vision of European science a generation before the establishment of the European Molecular Biology Organisation in the 1960s.

Great Britain and France were the major beneficiaries of RF's support in the biomedical sciences, especially in the provinces where RF's untiring scouting for new investment sites contrasted with the often modest state support to provincial scientists. RF's support of biophysicist turned molecular biologist William T Astbury at the University of Leeds for two decades, and of biochemist Emile Terroine at the University of Strasbourg, illustrates one of the most positive features of RF's willingness and ability to outreach into peripheral biomedical research communities. A similar observation holds for small European countries, such as Denmark, Holland and Hungary, which also enjoyed long-term RF support of biomedical science and was later to produce members of the founder generation in molecular biology.

By contrast, RF's investments in other large European countries, most notably Germany, Italy and Spain, were almost entirely curtailed by the rise of Fascist regimes. Although RF retained its 'apolitical' stance and continued its site visits in those countries' biomedical research establishments until the United States joined the war effort, it could not continue its usual operation, let alone its scouting for long-term and large-scale investment opportunities, because too many of RF's scientist grantees were expelled (Gemelli, 2000). As a result of racial legislation that led to the dismissal of many biomedical scientists, RF became involved in rescuing scientist refugees, not so much for humanitarian reasons but because RF considered the best scientific minds of Europe to represent a particularly valuable form of scientific capital. RF was particularly concerned about its own grantees, often succeeding in placing them in good positions in the United States, for example, the physiological geneticist Boris Ephrussi of France (placed at The Johns Hopkins University), Max Delbruck of Germany (placed at Vanderbilt University) and Salvador Luria of Italy (placed at Columbia University). Some of RF's grantees were placed at rather great distance, as for example Rene Wurmser, a biophysicist from the Institut de Biologie Physico-Chimique in Paris and a long-term RF grantee whom RF helped get an appointment in Rio de Janeiro for the duration of Second World War. **See also**: Bioethics – Overview; Eugenics: Historical

During Second World War, unmobilised biomedical scientists, including women and refugees, were among RF's most important beneficiaries. For example, the would-be Nobel Laureate Dorothy C Hodgkin of Oxford used RF grants most judiciously to employ vulnerable research assistants such as women students and refugees as well as to solve the structure of penicillin. Max Perutz, a would-be Nobel Laureate whose work on haemoglobin structure was made possible before and during Second World War by RF grants to his PhD adviser, Sir Lawrence Bragg, The Cavendish Professor of Physics at Cambridge, continued to benefit from RF grants after Second World War. This continued even after the British Medical Research Council (MRC) assumed responsibility for an emerging unit for biomolecular structure at the Cavendish Laboratory in Cambridge (Abir-Am, 2002). In addition to unmobilised biomedical scientists in Great Britain, other RF beneficiaries during Second World War included scientists from 'neutral' countries, most notably Sweden, where the inventor of the ultracentrifuge, the Nobel Laureate Theodor Svedberg at Uppsala University, remained a major RF grantee for a quarter of a century. **See also**: Hodgkin, Dorothy Mary Crowfoot; Medical Research Council (MRC); Perutz, Max Ferdinand; Svedberg, Theodor; The Status of Women in the Life Sciences

After Second World War, RF resumed its European operations, seeking to continue its pre-Second World War policy despite the fact that the international arena in science funding had greatly changed, with many new players outpacing RF in terms of their speed, size and willingness to cooperate with new governmental agencies established during and after Second World War. A pre-Second World War RF grantee from the Institute for Phsyico-Chemical Biology in Paris, Louis Rapkine, who had coordinated the rescue of French scientists on behalf of the Free French Forces during Second World War, was instrumental in RF making post-Second World War grants, especially for equipment and conferences, or aspects adversely affected by the war, not only to individual scientists but also to the governmental agency Conseil National pour la Recherche Scientifique (CNRS) for distribution all over the country. Although such a decision was primarily influenced by RF's need to distance itself from potential grantees who had been discredited by their collaborationist record during Second World War, it stands as one of few examples in which RF, a private philanthropy par excellence, dealt with governmental agencies (Appel, 2000; Gemelli, 2000, 2001; Krige, 2006; Picard, 1999; Schneider, 2002).

In Great Britain too, RF resumed operations interrupted by the Second World War mobilisation of its grantees, while consulting with its MRC. RF's long-term support of biomedical scientists in France and Great Britain before and after Second World War may have played a key role in these two countries winning eight out of nine Nobel Prizes in molecular biology until the late 1960s, after which the United States emerged as the most frequent winner. By 1953, RF decided to shift its entire philanthropic effort to agricultural development in Latin America (Cueto, 1994) and population studies in the Third World (Weindling, 2001), gradually phasing out its investments in biomedical science by the late 1950s, although not before it provided one of its star grantees, Boris Ephrussi, by then Professor of Genetics at the Sorbonne with a last, long-term, large-scale grant for his Laboratory at Gif-sur-Yvette on the outskirts of Paris, a laboratory built by the CNRS and equipped by RF. **See also**: Centre National de la Recherche Scientifique (CNRS)

By that time, the US, British and French governments were all turning to the support of biomedical sciences as part of a national science policy. RF's once unique position would have been soon eroded had it not decided to shift its priorities to agriculture in Latin America and the Third World. Indeed, RF obsessed a great deal about the impact of governmental massive funding of science during the Cold War on its own operations, to the effect that its Program in the decade after Second World War focused almost entirely on pre-Second World War grantees. This occurred even though National Science Foundation (NSF), the US main science funding agency, began to operate in 1950 only and picked up momentum in the late 1950s only (i.e. after the Sputnik) (Abir-Am, 2010; Appel, 2000; Kevles, 1977; Krige, 2006).

In addition to its international scope, which essentially meant that RF created an integrative, quasi-global network of scientific intelligence in biomedical research, including the United States, Europe, Latin America and the Far East (Abir-Am, 2001; Schneider, 2002), RF's new biomedical policy was uniquely innovative as a result of its built-in interdisciplinary character. RF's decision to focus on biology, as the science of life most conducive to social returns, did not mean that all fields of biology would be equally supported. Weaver's own background in engineering (he taught at Caltech and the University of Wisconsin) meant that he considered technology to be the most lasting achievement of scientific progress. Similarly, his scientific positivism and conservative social outlook meant that he regarded the orderly classical mathematical physics as an ideal to be emulated by biology, which he saw as 'backward, lacking laws and irrational'.

This slightly outdated philosophy of science (by the early 1930s, quantum physics had overthrown the key tenets of classical physics to which Weaver and his policy still clung, most notably rationality and causality) to which Weaver added organisational constraints within the RF, such as the need to demonstrate a visible departure from the previous policy that had focused almost entirely on physical sciences, became the basis of a policy that revolved around 'technology transfer' from the exact sciences to biology. In Weaver's definition, RF's Division of Natural Sciences would support neither physical science nor biomedical science, but only projects engaged in applying physical, chemical or mathematical techniques to biological material. This essentially meant that RF's officers determined eligibility for grants in terms of monitoring the grantees' purchase and use of modern laboratory equipment. Their policy had no other way, other than collecting professional gossip, to assess whether grantees worked on significant problems or kept track of changes in the scientific frontier. **See also**: Philosophy of the Life Sciences

This policy worked well in its early days, encouraging bold moves by physical scientists, who alone possessed the 'progress guaranteeing' physical techniques, into biological territory. Notable examples included the X-ray crystallographers William Astbury and Dorothy Hodgkin and their students in Great Britain; the spectroscopist of respiratory enzymes David Keilin at Cambridge University, one of few long-term RF grantees actually trained in biology (Abir-Am, 2002); Theodor Svedberg and his school of ultracentrifuge users and Arne Tiselius's group in electrophoresis (Kay, 1988; Kohler, 1991; Abir-Am, 2001), both in Sweden; Niels Bohr, Georg von Hevesy and August Krogh's project on using artificial isotopes in chemical reactions and physiological processes, in Denmark and Linus Pauling and his school of quantum and structural chemistry in the United States. In some cases, RF identified several suitable grantees in one institution. For example, at the Institut de Biologie Physico-Chimique established in Paris in 1927 by the Rothschild Foundation, RF's grantees included the biophysicist Rene Wurmser, the cell biochemist Louis Rapkine, the physiological geneticist Boris Ephrussi and their Director, the physiologist Andre Mayer. **See also**: Gel Electrophoresis: One-dimensional; Hevesy, Georges de; Pauling, Linus Carl

Impact on Life and Biomedical Sciences

The main achievement of this integrative, interdisciplinary and international policy, which continued for a quarter of a century (1933–1958) while spending US$90 million, was to precipitate within 5 years a new discourse on protein structure, a supramolecular and subcellular new, hybrid object that belonged to or rather challenged the traditional boundaries of both the life sciences and the physical sciences. On the one hand, its precise structure was attempted by many scientists using the above-mentioned physical techniques, as if the huge proteins were fully defined molecules; on the other hand, proteins' functions were investigated as biological and biomedical processes because they played a key role in respiration, digestion, reproduction and immunity. Macromolecules such as proteins pushed the life and biomedical sciences into a new level of biological order, the subcellular or the supramolecular, causing Weaver and his RF colleague, Wilbur E Tisdale, to coin the term 'molecular biology' for this new discourse on protein structure in the RF's Annual Report for 1938. **See also**: Protein Structure Classification; Protein Structure Design and Engineering; Protein Structure Prediction

One of RF's grantees, the mathematician turned theoretical biologist Dorothy Wrinch of Oxford, soon proposed the first theory of protein structure, a theory that unified findings produced with a multitude of RF-sponsored techniques, in half a dozen countries. The debate over the first theory of protein structure raged worldwide in the late 1930s, with JD Bernal, a physicist, and L Pauling, a chemist, as the other leading protagonists each striving to propose such a theory, in a fierce race for the 'secret of life'. Their debate defined the conceptual space that came to be occupied by molecular biology since the 1930s. That conceptual space was defined by three techniques from the exact sciences (X-ray crystallography, structural chemistry and topology) vying to capture the 'secret of life' in a direct reflection of RF's policy of technology transfer, a policy that appeared to precipitate a new, integrative and revolutionary discipline. **See also**: DNA Topology: Fundamentals; Time-resolved X-ray Crystallography

The effectiveness of RF's policy in sustaining scientific innovation in the biomedical and life sciences was determined in the long run not only by various technical limitations in solving the problem of protein structure in the era preceding the availability of computers nor by resonance with a quest for social stability, a quest drastically transformed by the outbreak of Second World War that redefined the world in terms of a polarised confrontation between two superpowers, and thus greatly emptied RF's cornerstone notion of political neutrality in international affairs (Abir-Am, 2010; Krige, 2006; Tournes, 2006). Equally important turned out to be the various investment instruments utilised by RF in pursuing its policy as well as internal organisational constraints on its concept of risk taking.

The new policy's most promising investment instrument was the targeted research appropriation for projects falling within RF's objective of supporting the application of physical techniques to biological material, especially because instruments such as fellowships and small grants-in-aid continued the tradition established in the 1920s. By contrast, the targeted research appropriation that evolved by the mid-1930s into long-term (five years) support had the potential to make a difference because it could steer the direction of scientific progress, as, for example, in the case of Linus Pauling of Caltech who began structural studies of bioorganic molecules in a clear response to opportunities for long-term and large-scale support from RF; or Niels Bohr at the Institute for Theoretical Physics at the University of Copenhagen who began studies of artificial isotopes in chemistry and biology, also in response to RF's interest and its own desire to accommodate the refugee scientist Georg von Hevesy, a future Nobel Laureate. **See also**: Hevesy, Georges de

However, RF's new concern with accountability in the aftermath of the Great Depression meant that tight regulations replaced the previous distribution of large sums of money to a few meritorious recipients, both individuals and institutions, in the manner of personalised gift giving, which expected nothing in return except for a vaguely defined adherence to scientific progress, as had been done during the 1920s. Devised by Weaver, a protégé of RF's President Max Mason (who held office from 1930 to 1936), the new regulations led to the distribution of grants to larger numbers of grantees according to criteria of eligibility defined in terms of pertinence to RF's own policy definition.

In this sense, RF prefigured post-Second World War governmental science policy of outreaching deeper into the scientific community, although the old system prevailed in the prerogative of RF's officers to solicit applicants as well as solely determine whether a scientist's project qualified for support. Even in such cases, compliance with various bureaucratic rules meant periodical monitoring of the grantees. For example, Weaver complained to Raymond Fosdick, RF's President in the late 1930s, that one of the leading physicists of the time, Niels Bohr, spent the larger part of his grant on physics instead of biology; Fosdick replied that when scientists such as Einstein, Bohr or Rutherford accepted RF's grants, there was no need to ask further questions. This story illustrates the danger of a policy degenerating into a goal in itself, instead of being a flexible means for the pursuit of scientific progress.

At the same time, the policy of grant distribution according to eligibility criteria was subjected to organisational constraints, for example, the delicate balance of power between the trustees, who remained the legitimate policy-makers, and the officers, who acquired the power but not the authority to make new policy. This meant that some officers, especially Weaver, favoured 'chicken feed' (Alan Gregg's term; Schneider, 2003; Abir-Am, 1982, 1995) as a less risky form of new investment, with the effect that only established as well as entrepreneurial scientists were likely to receive long-term and large-scale support, or the only type of support that could have had a sustained impact on scientific change.

RF's desire for exaggerated institutional guarantees often squeezed out junior innovators, as, for example, in the case of Joseph Needham and CH Waddington's project in physico-chemical morphology at Cambridge University. In this instance, RF revoked its initial support for junior innovators who perfectly fitted RF's criteria, simply because they could not secure patronage at their politically complex institution or were considered controversial by British science policy-makers for political and personal rather than scientific reasons. By contrast, institutional entrepreneurs such as Bohr, Pauling and Ephrussi received large-scale RF support even when their research only indirectly fitted RF's own criteria. Indeed, RF's strategy for containing risk created an infrastructure of entrepreneurial scientists who would pioneer 'big science' in the life and biomedical areas since the 1960s, a trend that culminated with the rise of the biotech industry and the Human Genome Project in the 1980s. **See also**: Needham, Joseph; Sequencing the Human Genome: Novel Insights into its Structure and Function

Yet, the effectiveness of RF's policy in the biomedical sciences was also determined by its institutional choices, especially medium-sized entrepreneurial institutions that attracted a great deal of foundation support (e.g. Cornell, Princeton, Caltech and Stanford in the United States and Uppsala, Copenhagen, London, Cambridge and Paris in Europe). By contrast, in the post-Second World War period, the long prevailing paradigm of a structural molecular biology centred on proteins gave way to informational molecular biology centred on deoxyribonucleic acid (DNA) as well as to a new institutional ecology focused on the MRC Laboratory in Cambridge, the Pasteur Institute in Paris, the Cold Spring Harbor Laboratory in New York and the European Molecular Biology Laboratory (EMBL) in Heidelberg. **See also**: Cold Spring Harbor Laboratory; Institut Pasteur and Satellite Institutes; Medical Research Council (MRC)

Paradoxically, RF key grantees who received long-term and large grants ended up losing their former, pre-war pioneer positioning on the biological frontier in the post-war era, when the centre of gravity of world science shifted to the United States. As such key grantees remained locked into a pattern of sponsorship that monitored technology transfer only (i.e. the use of physico-chemical techniques on biological material), they were slow to notice the shifts in the biological frontier in the post-Second World War era from structure to function, from proteins to nucleic acids, from organisms to microorganisms, from institutional rigidity to individual mobility and from classical to molecular biology (Abir-Am, 1982, 2002, 2010; Abir-Am *et al.*, 1984).

For example, key grantees such as William Astbury in the United Kingdom and Linus Pauling in the United States, whose mini-research empires epitomised two decades of RF investments through its core policy of technology transfer, continued to prioritise protein structure studies well into the early 1950s, when DNA structure was shown to explain functions previously attributed to proteins, while inducing a paradigmatic shift from conformational to informational biology. As recent studies on 'history and memory' suggest, the placement of RF's grantees as leaders of molecular biology is a product and artefact of commemorative practices. Ironically, despite a promising start at a key historical junction, RF's policy in the biomedical and life sciences may have done more to shape the rise of 'big science' in these fields rather than fostering the collaborative innovation that became a hallmark of molecular biology in the post-Second World War era. **See also**: DNA Structure Changes Coupled to Protein Binding; History of Molecular Biology

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