



Developing Successful Models for Large-Scale, Collaborative Biomedical Research Projects

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While biomedical research has led to cures for many previously intractable diseases, a class of diseases caused by complex interactions of genetic and environmental factors has defied both understanding and cures. These complex diseases, including cancer, multiple sclerosis, adult onset diabetes, schizophrenia and hypertension, are currently treated by managing disease symptoms, not by addressing the diseases' root causes. The difficulty in addressing these diseases has been largely due to the high degree of complexity of the problem.

The challenge in trying to cure complex diseases is the challenge of solving a puzzle whose pieces are discovered through research in a multitude of disciplinary approaches. Putting the puzzle together will require the ability to join information at the interface of these disciplines. Such an undertaking would have the greatest chance of success if experts across a variety of fields of research were to join their efforts in a large, cross-disciplinary collaboration. However, such collaborative approaches to biomedical research have been surprisingly infrequent.

This paper will first explore the examples of two highly successful large-scale scientific projects in order to identify the factors that contributed to their success. Next, it will discuss various factors that may work for or against the creation of interdisciplinary biomedical collaborations. Finally, strategies for facilitating the creation of large, collaborative biomedical research projects will be discussed.

The Manhattan Project

One of the most celebrated examples of a large-scale scientific collaboration is the successful development and manufacture of the atomic bomb. The Manhattan

Project was the first large-scale applied science project of its kind. It had an explicit objective (to build the bomb), an enormous budget (over \$2 billion 1940's US dollars), and aggressive deadlines (required by the war effort). Its success relied on an unprecedented level of theoretical and technical innovation; nearly all the technology used in the design and manufacture of the bomb needed to be developed.

The Manhattan Project drew on the creative capabilities of the greatest minds in physics of that, or possibly any generation. Robert Oppenheimer, Albert Einstein, Neils Bohr, Edward Teller, Enrico Fermi, and Richard Feynman were just some of the extraordinary physicists who labored on the project, along with hundreds of other physicists and thousands of engineers and support staff. Despite miserable living conditions¹, extremely difficult logistics², and a difficult, often openly contentious partnership between civilian scientists and military engineers³, the project succeeded. How was it possible to keep such a challenging project on track for the three years required to develop the bomb?

The Manhattan Project survived and eventually succeeded in large part due to the exceedingly high degree of motivation of the participating scientists. This motivation derived most importantly from their shared conviction that the Allies needed to develop the bomb before Hitler did. Many of the physicists involved in the project were Europeans who had been forced to flee their homelands. Neils Bohr, for example, had been smuggled out of Denmark at great risk just before the Germans' advancing army⁴. For the Americans, support of the war effort was an equally strong motivator. The need to win the race against Hitler created a constant state of urgency that drove the scientists to work despite exhaustion, difficulty, great personal sacrifice and real personal danger.

However, there were other sources of motivation as well. For physicists interested in nuclear physics, no other project could have offered a comparable level of excitement, professional and personal satisfaction. The Manhattan Project was an extraordinary challenge, an "intellectual match between the scientists and the cosmos"⁵. It would represent the culmination of a half- century of exceptional advances in the field of nuclear physics by the Curies, Becquerel, Rutherford,

Einstein, Bohr, Fermi and others. It was a unique opportunity to test their theories on a grand scale and to advance the field.

The Manhattan Project brought together a large community of scientists and engineers, including the greatest physicists of the age, in an active collaboration. For the young physicists, it was an incomparable opportunity for professional development; they would have the opportunity to learn by working with the giants of their field. For the leading physicists, it was an opportunity to realize their vision by putting theory into practice. Recognition of a scientist's or engineer's good work by their peers would have extraordinary value in this community and would have been a source of continuous motivation. The scientists also shared a spirit of camaraderie, working long hours together during the day and socializing together at night. Their joint suffering with the privations of their uncomfortable working and living conditions drew the members of the community together.

In addition, motivational support came from no less than the President of the United States. During the course of the project, Franklin Roosevelt personally sent a letter of encouragement and support to the scientists to help maintain their morale⁶. Finally, the scientists were motivated by their deep respect for the project's leader, J. Robert Oppenheimer. This respect was earned not only by his genius in theoretical physics, but by his kindness to and support of the scientists in his charge. Oppenheimer was the glue that held the scientists together, melding them into a team. The men under Oppenheimer likened him to a football coach, "because he had the ability to organize them as a team and make them play their hearts out"⁷.

Beyond the participants' own motivation, there were considerable external sources of pressure that drove the project forward. The engineers were members of the military and as such, had no choice as to their level of participation in the project. The head of the Los Alamos laboratory complex was General Leslie Groves, who was accountable to Washington for the project's progress. In addition to his commitment to the war effort, Groves' career was at stake; success would mean accolades and advancement while failure would be ruinous⁸. Groves oversaw the logistical support for the project and provided managerial oversight; he also provided continuous pressure to keep the project on target.

No amount of motivation and external pressure would have resulted in the successful development and manufacture of the bomb had the resources to support the project not been available. The Manhattan Project was given such high priority (double-X priority) that project members had the ability to divert critical resources from other parts of the war effort if needed⁹. The project involved not only the complex at Los Alamos, but supporting facilities at Oak Ridge, Tennessee and Hanford, Washington which were responsible for refining Uranium 235 and producing plutonium to be used in the bombs' manufacture¹⁰.

In the decades that followed the Manhattan Project, large-scale collaborative projects in applied physics and engineering became more common. The NASA projects, starting with the Mercury and Gemini projects and culminating in the Apollo missions, shared many common traits with the Manhattan Project. For the participants in these projects, the high level of motivation also resulted from a combination of strong professional interest and patriotism, here stimulated by the Cold War. Following the shock of the Sputnik launch, the United States was determined to recapture its lead in space, a commitment that led to President Kennedy's dramatic goal of landing men on the moon. This meant that the NASA projects were a national priority, receiving funding and support from the President on down. This high level of government interest also meant extremely high visibility and external pressure to succeed.

Less visible, less political projects were also created with objectives that were more purely scientific. These included the creation of a number of international astronomical observatories, as well as the international collaboration to build and share the large-scale facility for nuclear physics research, CERN. The extreme cost of such facilities was an obvious incentive for nations to pool their resources in order to make possible advances in these fields. The research performed at these facilities, however, is not necessarily collaborative, with research teams reserving time at these facilities in order to pursue individual projects that are often competitive with projects of other research teams.

The Human Genome Project

The field of biomedical research has evolved from the individual efforts of doctors, scientists, artists (Da Vinci) and monks (Mendel) whose careful observations and creative experimentation have shed light on pieces of the great puzzle of life. The history of biomedical science is replete with heroic discoveries by inspired individuals. These discoveries often involved the observation of something unexpected and unplanned. An example of such a discovery is Alexander Fleming's observation that bacterial cultures had been cleared in some petri dishes accidentally contaminated with mold, which led him to the serendipitous discovery of penicillin¹¹.

Due to the great complexity of life, attempts to understand it became segmented into a variety of approaches organized by scientific disciplines such as biology, chemistry and physics, and medical disciplines such as anatomy, physiology and pathology. As the amount of knowledge increased, new specialties were formed such as immunology and cell biology, where practitioners could deepen the understanding in a particular system or level of biological organization. As discoveries pushed scientists into realms where disciplines began to merge, new interdisciplinary fields were created: biochemistry, biophysics, and biomechanics to name a few. However, biomedical research continued to be pursued predominantly by individual research labs focusing on small pieces of the much larger puzzle.

In 1971, President Nixon attempted one of the first major biomedical research initiatives, declaring his War on Cancer. The National Cancer Act involved the expansion of the responsibilities of the National Cancer Institute and the allocation of \$100 million of additional funding for cancer research¹². While progress was made, it was much slower than expected. This was predominantly due to the complexity of cancer as a disease, requiring knowledge and tools that would not be available for another decade to come. It was only in the 1980's that critical technological advancements such as recombinant DNA and laboratory computers became common tools of biological research.

It was against this backdrop of change that the most audacious project in biomedical research came into being. The Human Genome Project was a radical departure from previous research approaches. It was the first attempt at Big Biology

– a large-scale, targeted project that by its end would involve the collaborative efforts of 16 principal and many more small-scale genetic sequencing centers across the world. It would involve the efforts of scientists from a broad number of fields – biologists, mathematicians, statisticians, computer scientists and engineers. The project would also require the development of new technologies – new biochemical methods for tracking DNA, new, sophisticated computational algorithms for aligning sequences, and new automated equipment that could increase sequencing productivity to the point where the project would be feasible from the perspectives of both time and cost.

In addition to its being a spectacular achievement, the Human Genome Project became a drama of human intrigue and conflict, first pitting one government agency against another and then pitting a public consortium against private, commercial interests. The project's success can be attributed to a complex mix of human motivations and supporting factors.

Currently hailed as a great achievement and the promise of revolutionary changes in the drug industry, the Human Genome Project was first met with a great deal of skepticism. Robert Sinsheimer, then chancellor of the University of California at Santa Cruz, gathered a group of leading molecular biologists in 1985 to propose his idea for a project to sequence the human genome. The responses were mixed but predominantly negative. The members of the gathering acknowledged the attraction of this bold vision; however they felt that given current technology, it simply could not be done¹³.

While the technology existed in 1985 to sequence genes, the process was painfully slow; sequencing of the Epstein-Barr virus, which was only 1/20,000th the size of the human genome had taken several years to complete¹⁴. Aside from the general belief that the project was simply not feasible, members of the scientific community raised a number of additional objections:

Financial concerns: Many scientists were concerned that a project of the proposed magnitude would monopolize all federal funds allocated for biological research. The projected cost was over \$3 billion. In addition, while agreeing that the sequencing of genes would be valuable, many scientists were not convinced that it

was worth the cost to sequence the entire human genome given that over 98% of human chromosomes is comprised of “junk” DNA, i.e. DNA that does not code for genes¹⁵.

Professional concerns: Due to the painstaking, repetitive work required to sequence genes, some opponents feared that a generation of young scientists would become slaves of tedium. As an expression of this concern, “Sydney Brenner . . . facetiously suggested that project leaders parcel out the job to prisoners as punishment – the more heinous the crime, the bigger the chromosome they would have to decipher”¹⁶.

Cultural concerns: Many scientists objected to the idea of research projects taking a “big biology” approach. They adhered to the prevailing belief that “the best work . . . came from investigator-initiated studies in small labs, not from some massive, goal-driven effort”¹⁷.

Given the range and depth of these objections, how did the Human Genome Project gain sufficient support to become a reality? One key was Dr. Walter Gilbert. Dr. Gilbert, a leading scientist who later received the Nobel Prize for his research in genetic sequencing, became the Human Genome Project’s biggest proponent. Once he placed his reputation behind the project, it was given sufficient credibility to gain the serious consideration of the scientific community¹⁸.

In addition, the project gained a critical champion within the federal government. Charles DeLisi, then head of the Office of Health and Environmental Research at the Department of Energy. For Dr. DeLisi, the Human Genome Project had the potential to address a critical need within his department: “a massive new endeavor could provide new focus for DOE’s national labs, whose bombmaking skills were in diminishing demand”¹⁹. In 1986, Dr. DeLisi hosted a workshop to discuss the potential for a human genome project, and the idea began to gain momentum²⁰. While the NIH showed no inclination to support the Human Genome Project, DeLisi argued that the DOE was the best agency to support the project given its experience in managing “big science” projects, experience that the NIH lacked²¹.

The project finally achieved a consensus of support from a National Research Council (NRC) panel comprised of both proponents and opponents of the Human

Genome Project who defined a phased approach to tackling the sequencing of the human genome that they all endorsed²². The phased approach called for initially mapping the human chromosomes and sequencing the genomes of smaller organisms in order to have a source of comparison.

While some praised this methodical approach, the slow pace that it would dictate frustrated others. Walter Gilbert was the first to break with the public effort of sequencing the human genome. He left the NRC panel to start a private company called Genome Corporation whose objective was to sequence the human genome directly and then make the information available for a fee. While failing to raise sufficient funding, he anticipated both the later commercial success and vilification by the scientific community of Celera Genomics²³.

Once the Human Genome Project had achieved the support of the scientific community and funding from Congress, the NIH finally decided that it was interested in running the show. In 1988, the NIH created a special office for genome research and secured as its director James Watson, one of the Nobel laureates famed for determining the structure of DNA. This move allowed the NIH to successfully wrest control of the project from the DOE²⁴.

It turned out that Watson was an excellent choice to head the NIH special office. Watson was highly successful at dealing with Congress, being “skilled in the care and feeding of those who controlled congressional purse strings”²⁵. He was extremely conscious of the political climate influencing the project’s financial support. Fearing that Congress’ lack of patience could jeopardize the flow of funding needed to take the project to completion, Watson staked his reputation on the project’s ability to create maps of the human chromosomes in 5 not 15 years, and successfully drove this first phase of the project to meet this deadline²⁶.

It was at this stage with the project beginning to make serious progress, that Dr. Craig Venter injected the first of what was to be many disruptive episodes. Venter, then a member of the National Institute of Neurological Disorders, was not part of Watson’s inner circle and lacked the ability to influence the project’s direction. When Watson failed to support his proposal for an accelerated identification of the portion of the genome coding for genes using expressed sequence tags (ESTs), a

new technology that he had developed, he went public with his plan, making broad claims of his rate of progress, his ability to file patent applications on the genes he had identified and the NIH's enthusiasm for his work. Outraged, Watson publicly denounced Venter in front of Congress. In the fall-out of this imbroglio, Watson left the NIH²⁷.

This episode ultimately led to Venter's leaving the NIH for the first of two private efforts to sequence the human genome. In 1991, Venter joined the Institute for Genomic Research, a non-profit organization with \$70 million of venture capital funding. In 1995, TIGR succeeded in sequencing the entire genome of *Haemophilus influenza* in a single year, a feat only made possible by a new approach called whole-genome shotgun sequencing that the NIH had rejected as unfeasible²⁸.

By contrast, the NIH effort had been slowing down. Prior to TIGR's success, Dr. Francis Collins, Watson's replacement, had even expressed doubts about the project's ability to be completed by the 2005 target due to the failure of expected technological innovation to be developed²⁹. Despite TIGR's example, Collins persisted in advocating the methodical approach that the NIH had been pursuing from the outset. The NIH only abandoned this slow and steady approach after Venter teamed up with Perkin-Elmer Corporation to form Celera Genomics, spurring a race between the public consortium and Venter's group³⁰.

In 1998, Venter claimed that, using whole-genome shotgun sequencing, Celera Genomics would be able to sequence the entire human genome in a scant three years for the bargain basement price of \$300 million³¹. Leaders of the public project were incensed; "(a)fter they had spent years laying the groundwork, could Venter really beat them to the finish and steal the glory?"³². In addition to feeling anger, the heads of the public effort were also fearful that Venter's claim would cause Congress to withdraw financial support of the public project.

The NIH responded by a radical change in policy. The Human Genome Project would produce a "rough draft" of 90% of the human genome by 2003. While ostensibly this change was intended to make sequence information available to the scientific community more rapidly, Collins admitted that the shift was also intended to "undercut any patent position Celera or other businesses might claim"³³.

From 1998 on, the two sides competed both in their efforts to complete the sequencing of the human genome and in their efforts to influence public opinion. A flurry of press releases issued forth from both sides as each side achieved critical milestones. As the level of acrimony between the NIH and Venter escalated, Eric Lander, head of the Whitehead Institute's Genome Center, attempted to mediate between the two sides in order to establish collaboration rather than competition between the public and private groups. Despite these efforts, the only agreement reached was that both sides would publish their final sequences at the same time in February of 2000³⁴.

However, they could not even agree to publish in the same journals, due to concerns within the scientific community that the Celera publication would not satisfy the requirements of peer-reviewed papers. This concern centered on Celera's insistence that access to the raw data supporting the paper would be restricted to academic labs with no commercial connections and commercial laboratories that paid Celera's access fees. Given that many academic labs have extensive connections to biotechnology and pharmaceutical companies, many leading scientists were concerned that many top geneticists would be prevented from reviewing the data on which the Celera publication was based³⁵. As a result, the NIH-backed project published its findings in *Nature* while Venter's group published its findings in *Science*.

Despite the divisiveness that characterized much of its history, the Human Genome Project is a major scientific achievement, opening the door to many new opportunities for basic science and biomedical research. It has also created a critical precedent for large-scale collaborations for biological research as well as important methods for the creation of shared repositories of scientific data. With the success of the Human Genome Project, a large number of collaborations are currently under way to create new public databanks of genetic and protein sequences.

Many of the genome research centers that had participated in the Human Genome Project are launching new projects to sequence the genomes of a wide variety of organisms from puffer fish to parakeets. Current projects also include the SNP Consortium, a collaboration of 11 major pharmaceutical and technology companies and four major centers of genomic research, which is attempting to

identify all single nucleotide polymorphisms or mutations found in the human genome³⁶.

In addition, data sharing efforts are beginning to focus on the pooling of disease-specific data. For example, the Alzheimer Research Forum provides the research community with updated directories of genetic mutations and relevant research findings³⁷. This latter direction will have important applications for the research of complex diseases.

Key Factors of Success

What can be learned from these two groundbreaking projects in large-scale scientific innovation? While the Manhattan Project and the Human Genome Project differed significantly in terms of purpose and motivations, several key factors were common in helping to create the conditions for success.

For both projects, the mission was visionary, capturing the imagination of their respective scientific communities. The potential payoffs resulting from the projects' success were understood to be spectacular. For the Manhattan project, that payoff was the creation of the greatest weapon in existence, providing the Allies with the means to end a devastating war. For the Human Genome Project, the payoff was the "Book of Life", the complete human genetic code that would allow scientists to unlock the secrets of mankind's most challenging diseases. The visionary scope of these projects helped attract both the best scientific talent and the continued financial support of the federal government despite the projects' staggering technical hurdles.

At critical times, both projects benefited from the leadership of respected, charismatic figures. For the Manhattan Project, Robert Oppenheimer held together a coalition of independent, opinionated thinkers and drove it unswervingly towards the project's goal. For the Human Genome Project, several figures played key roles at different stages of the project. Walter Gilbert provided critical leadership in building support for the project from a dubious scientific community. James Watson provided the leadership necessary to maintain the flow of critical resources from the federal government and lent his prestige to the project, enhancing its credibility with the lay

community. Finally, Craig Venter, by providing the driving force for the development of key technical innovations and the creation of a serious threat of commercial dominance of the human genome, galvanized both the private and public efforts for the completion of the Human Genome Project.

Venter's contribution included another key factor common to both projects – an important sense of time urgency. Prior to Venter's challenge, the Human Genome Project had been losing ground with respect to its original timeline. It can be safely argued that the threat of Venter's winning the race provided the impetus for the public consortium to intensify its own efforts as it sought to prevent Venter from being the first to complete the sequencing of the human genome. This resulted in a radical shortening of the time needed to complete the project. It is even possible that, had Venter not challenged the public consortium, the Human Genome Project may have lost government support as it failed to adhere to its timeline.

For the members of the Manhattan Project, the sense of urgency stemmed from issues of immediate life and death. Project members felt a direct responsibility initially for the success of the war effort against Hitler and later for preventing the wholesale slaughter of American soldiers that was anticipated in the event of an invasion-force being sent to Japan. In addition, continuous pressure was applied by military and government leaders who needed the project to succeed on a time frame dictated, not by the pace of normal technical advances, but by changes that would determine the political and military outcomes both of the war and the post-war landscape. Due to this time urgency, project members worked ungodly hours, pushing themselves to meet the deadlines to which they had committed themselves.

Both projects were enabled by substantial political and financial support from the federal government. In addition to the involvement of federal agencies and support of government champions, the federal government provided the funds to cover the projects' enormous budgets. Its continuous supply of funding was absolutely essential for these large projects to be completed.

Probably the most important factors enabling their realization were the intense human motivations of the various players involved in the creation, implementation, funding and performance of these projects. For project participants, work involved

intensive, sustained efforts in the face of enormous odds. In the case of the Manhattan Project, participation involved great personal sacrifice and even personal danger. Strong emotional forces were necessary to overcome these obstacles. In both cases, these motivations included enthusiasm for the project's vision and the potential to advance both scientific knowledge and applications of great importance to humanity, great personal satisfaction from working on the project with other leading scientists, and the potential for great personal prestige and professional advancement should the project succeed.

In both cases, key government officials had strong political motives for supporting their projects. For the Manhattan Project, it was General Leslie Groves, seeing an opportunity for personal advancement. For the Human Genome Project, it was Dr. Charles DeLisi, who saw an opportunity to provide an important new role for the DOE.

Additional motivations were particular to the different projects. For the members of the Manhattan Project, patriotism and support of the war effort were enormous motivating factors. The European scientists had the added motivation of freeing their homelands from Nazi control. In the case of the Human Genome Project, motivations were not nearly so altruistic. For Walter Gilbert and Craig Venter, a key motivation was the opportunity for commercial success. For the members of the public consortium, key motivations included feelings of anger towards and betrayal by Craig Venter, leading to intense feelings of competition.

Implications for Large-Scale Biomedical Research Collaborations

The introduction to this paper described a pressing need for large-scale biomedical research collaborations that could determine the causes of complex, multifactor diseases like cancer. In order for such large-scale biomedical research projects to have a chance of succeeding, they need to incorporate those factors that appeared to be critical in the success of such projects like the Manhattan Project and the Human Genome Project.

It is vital to understand the micro-motivations of the research scientists who would be participating. As was discussed above, there are many factors that could provide strong motivation for scientists to participate in such collaborations. However, currently there are also many professional and economic factors that may discourage researchers from participating in such projects. In order to recruit scientists for such collaborations, these factors must be understood and addressed.

To begin with, professional accomplishment and economic security for an academic scientist usually involves achieving a tenured position at an institute of higher learning. The decision to tenure faculty is based in large part on the scientist's success in publishing his or her research, the famed "publish or perish" dictum. This pressure comes in two forms. First, there is a pressure to publish a large volume of work in recognized journals as a measure of the scientist's productivity. This will drive the scientist towards projects that are yielding positive results with the opportunity for a string of publications; conversely, it will drive the scientist away from difficult projects that will require years of efforts before publication is possible. Second, the decision to tenure favors faculty who have published research findings based on independent work in a well defined scientific discipline. This tendency has acted strongly against scientists who have participated in more collaborative, interdisciplinary research³⁸.

In the case of the many consortia that share DNA and protein sequence data on public web sites, there are additional challenges. Concerns regarding the protection of data that is posted in public databanks prior to publication are forcing the scientific and legal communities to rethink policy regarding intellectual property and public disclosures³⁹. The resolution of this issue will be critical in order to ensure the proper recognition of participants' efforts. In a recent article in *Science*, David Roos expressed the hope for "(i)ncreased acceptance of Web-based release as a form of publication (for hiring, promotion, tenure decision, etc.) as well as increased understanding of the nature of "big science" projects in biology, . . ."40.

The current trend towards commercialization of technology developed by academic labs has introduced an economic impetus to limit collaborative work. For those scientists drawn by the possibility of licensing patents based on their research

to biotechnology or pharmaceutical companies, the incentive is to minimize the number of patent authors in order to maximize the potential economic return. In addition, the increasing amounts of academic research supported by funding from commercial sources can create serious difficulties in the sharing of information in collaborative projects.

Less obvious but potentially of equal importance are the social forces that may play an important role in the interactions between the members of large collaborative projects. For academic researchers who value their autonomy, such projects have the potential to be quite threatening. There are several ways in which researchers may feel a loss of control in such a situation.

For a targeted research project, scientists may feel frustration at having to ignore interesting and potentially valuable serendipitous findings that are not directly related to the project at hand. Serendipity has been the source of new projects for many if not most research labs, with some finding the new projects to be much more successful than the original ones. The value of serendipity is embedded in the culture of the scientific community. The obligation to stay on track with a focused project would be counter to the practices and expectations of many researchers and may prove difficult to accept.

Another concern involves the dynamics between participants in a large-scale collaboration. Given differences in prominence based on career success, one or more members of the collaboration may be “more equal” than others. This can lead to problems for members both in terms of feeling like equal contributors and of receiving an equal allocation of resources.

Finally, some researchers might find the prospect of collaborating with scientists from outside of their field to be intimidating. Collaborations among biologists, chemists, physicists, mathematicians, statisticians and computer scientists and engineers require the creation of a common conceptual framework and a common language. Above all, they require mutual respect and patience among all participants.

Offsetting these issues are factors that can provide strong incentives for scientists to participate in large-scale biomedical research collaborations. To begin

with, strong personal interest in a particular disease can be a source of intense motivation. Such interest can be due to fascination with a particular problem and/or can be due to the impact that the disease has had on a researcher's family or friends, resulting in the strong desire to conquer the disease and find a cure.

Professional motivations can be equally important. As discussed above, the opportunity to collaborate with top scientists and the potential for great prestige and advancement associated with such projects can be highly motivating. Scientists interested in pushing the envelope of biological research may also be extremely interested in projects that involve interdisciplinary collaborations that have the potential of generating new sources of data and new forms of analysis. In addition, the potential for new commercial opportunities with their associated economic rewards will provide strong motivation for some researchers.

For such projects to succeed, it will be critical for the micro-motivations of the participants to be aligned with the overall goals of the projects. In addition, the projects should focus on incorporating other key factors such as charismatic leaders and champions and the financial support of government agencies or other entities capable of supplying large amounts of funding. In addition if aggressive timelines are to be met, some source of urgency whether internal and/or external will be needed in order to drive the project forward.

Finally, the success of the Human Genome Project has created the opportunity for substantial public support of future biomedical projects. The Human Genome Project achieved a level of public awareness and interest that far exceeds any previous effort in the biomedical arena. Leading figures from the Human Genome Project have become public icons, and expectations of medical benefits resulting from the project's completion are enormous. Future projects should make an effort to capitalize on the public approval of the Human Genome Project in order to generate political and financial support.

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