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The Stanford Institute for Chemical Biology

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Stanford University has recently launched the Stanford Institute for Chemical Biology (SICB), designed as a partnership between the School of Medicine, Humanities and Sciences, and Engineering. The core mission of the Institute is to strengthen the chemical foundations of human biology and to accelerate molecular discoveries that could ultimately transform human health. The Institute will foster an environment for learning across physical science, engineering, biology, and medicine and train future leaders who can traverse traditional disciplinary boundaries to explore problems that advance our understanding of human function. Those working under the aegis of the SICB will profit from an education that connects the time-honored principles of chemical structure, reactivity, and intermolecular forces with the formidable complexity of human biology. Such knowledge and collaboration will enable breakthroughs that transform the laborious, time-consuming, and expensive discovery and developmental processes that slow innovation in molecular science and medicine.

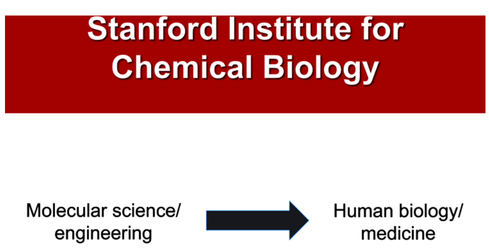

Figure 1. In essence, our expectation is to harness chemistry, defined broadly, to add value to the study of the newest entrant into the pantheon of model systems in biology – *Homo sapiens*.

THE OPPORTUNITY: CHEMICAL BIOLOGY OF *HOMO SAPIENS*

In the dawn of the post-genomic era, our species is poised to become a 'model organism' for biological study. Modern analytic technologies are revealing differences between humans at the level of single functional groups. Diagnostic science is, in effect, generating the molecular 'parts list' responsible for individuality. Armed with such information alone, the operating manual for *Homo sapiens* is, however, far from complete. To understand how these parts make the 'whole' – how the machine functions, how it ages, and how it can be properly repaired – we are at the mercy of chemistry.

The power of chemistry in the 21st century to control reaction outcomes in the regulated environment of the round-bottom flask has reached a level of sophistication that belies the complexity of the underlying physical science. Unfortunately, the same cannot be said for the design of reagents that act selectively to influence biological function. The complexity of the cell forces untold rounds of design → build → test in both discovery and development. While advances in high-throughput technologies have mitigated the burden of error, these methods do not fundamentally alter the error rate. To change this paradigm, chemists and engineers need to partner much more effectively with biologists and physicians. Such collaborations have the potential to take us beyond annotation, into the realm of quantitative input-output relationships that are not just predictive but also applicable at anatomical length- and physiological time scales. Compare, for example, the predictability of the UI/O (universal input/output) modules in a self-driven car with that of individual drugs and devices used to manage diabetes. Today, a prototype of only one of these complex systems can be invented through less than 10 design → build → test iterations. With the right kinds of intellectual partnerships, chemical biology can change that.

THE VISION: A CADRE OF "PHYSICIAN-SCIENTIST-ENGINEERS"

The pivotal role of a physician-scientist or engineer-scientist in molecular medicine is indisputable. Students having acquired such cross-disciplinary knowledge often have the intellectual temerity to lead science. Stanford is among a very small number of research universities that is home to exceptionally talented and accomplished physicians, biologists, physical scientists, and engineers working within a few minutes walk of each others' laboratories and offices. When coupled with the proximity of the SLAC National Accelerator Laboratory, home to some of the most advanced crystallographic resources including the unique X-ray Free Electron Laser for microcrystal-based, high-resolution structure determination, the environment is arguably one of a kind. SICB seeks to leverage the university's unique physical plan as well as the collaborative, risk-taking spirit encoded in its DNA, as it embraces emerging opportunities at the chemistry—human biology interface.

Over the next decade, the Institute will partner with departments in the Schools of Medicine, Humanities and Sciences, and Engineering to recruit approximately 20 new faculty to Stanford. These individuals will cohabitate a new building positioned at the nexus between the three schools and proximal to Stanford's hospitals. SICB scholars will likely fit one of the following profiles: a gifted molecular scientist/engineer who has turned his/her attention to important challenges in human biology, or an insightful biologist/physician who can frame human biology's most fascinating mysteries in a manner that lends itself to molecular analysis and design. Institute faculty will willingly subject their science to the standards of the disciplines that define the problem, not their field of expertise.

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They and their students will also be challenged to communicate effectively in multiple languages of science.

In parallel with the recruiting of top talent, the Institute is launching seed funding programs in selected thematic areas that bridge Stanford's chemical and biomedical communities. Entrepreneurial industrial scientists, such as medicinal chemists, who have an intuitive understanding of chemistry's value proposition to human biology, will be employed as research staff within the Institute. Their role will be to engage Stanford biologists and physicians in collaborations that are often not feasible between tenure-line faculty in traditional departmental structures. The availability of shared instrumentation that enhances not just the throughput but also the precision of molecular and pharmacological discovery will further enhance the creativity of this ecosystem.

In the aggregate, all of the above ingredients will give rise to a spectacularly powerful training ground for an entirely new breed of young "physician-scientist-engineers". These biomedical researchers will speak PyMol, love to tinker on a length scale a million times smaller than the width of a human hair, and combine their dedication to improving health with deference to the laws of thermodynamics. Their talent for molecular analysis and design, coupled with their passion for human biology, will allow them to lead what will arguably be one of the 21st century's greatest accomplishments – the final chapters of the *Homo sapiens*' "operating manual".

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