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Introduction

INTRODUCTION TO SPECIAL ISSUE

Translational glycobiology: Patient-oriented glycoscience research

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In his 1945 report to President Harry S. Truman entitled "Science: The Endless Frontier", Vannever Bush, the then-Director of the US Office of Scientific Research and Development, outlined his vision for a "National Research Foundation", which ultimately became the "National Science Foundation". In that document, Bush wanted to distinguish "basic research" from "applied research", and offered a plan to create a government-sponsored funding agency to promote scientific education and to provide grants to nonprofit organizations for the pursuit of basic research: "Basic research is performed without thought of practical ends. It results in general knowledge and an understanding of nature and its laws. This general knowledge provides the means of answering a large number of important practical problems, though it may not give a complete specific answer to any one of them. The function of applied research is to provide such complete answers" (Bush 1945). In drawing the distinction between basic and applied research, Bush emphasized that the latter is problem-inspired. Thus, applied research expressly seeks to provide solutions to specific problems, i.e., is *goal-oriented* to offer "complete answers" to "practical ends".

Applied research that is devoted specifically to addressing unmet medical needs is called "translational research". Analogous to other "-omics" (e.g., proteomics and genomics), glycomics is the comprehensive investigation of the structures, interactive pathways, and dynamic changes of glycans that impact biological systems, including both physiologic and pathologic processes. However, in the strictest sense, the term "glycomics" refers principally to the categorization/characterization/elucidation of the structures of glycomolecules (e.g., encompassing information generated via NMR and mass spectrometry analysis), while the expression "glycosciences" focuses on how glycan structures relate to biologic and chemical processes/properties. Seamlessly bridging these two realms, there exists a discipline which I call "translational glycobiology", a term, which I hold, refers to glycoscience-based research that is specifically motivated by the intent to alleviate human suffering, which is distinct from types of glycomics inquiry that are not patient-oriented and, also, differs from the application of an existing glycoscience-based technique or reagent in clinical medicine simply because someone clever realized its utility in that setting.

In this thematic special issue of *Glycobiology*, the field of translational glycobiology is highlighted through the first-person narratives of four authors, each of whom is an experienced clinician. It is hoped that these articles will be both enlightening and entertaining, as each author was encouraged to relay their personal research journey within the pertinent historical perspective(s). These authors represent four distinct areas of clinical medicine: (i) Cell therapeutics (Sackstein); (ii) Transplant surgery (Cooper); (iii) Internal medicine/Allergy & Immunology (Bochner); and (iv) Dermatology (Maytin). The first article provides a framework to evaluate the biologic activity of glycoconjugates, reviews the discovery of the CD44 glycoform known as "HCELL", and discusses how cell surface glycans can be custom-modified to optimize cellular delivery to predetermined anatomic sites and thereby enable the application of cell-based therapeutics. The second article addresses how glycans impact solid organ transplantation, and how strategies to alter expression of critical glycan determinants may pave the way to cross-species transplantation (i.e., xenotransplantation), thus overcoming the critical shortage of organs needed to save the lives of patients with organ failure. The third article describes the discovery of a sialoadhesin now known as "Siglec-8" and how our increasing understanding of the structure and biology of this molecule is yielding novel therapies for allergy and other immunologic diseases. The fourth article reviews our current information on the complex biology of the glycosaminoglycan hyaluronic acid, and how structural modifications of this molecule can be harnessed to improve wound healing and dampen inflammation, effects far broader than its more recognized role in cosmetic applications as a space-filler/wrinkle-remover.

There is no prerequisite that investigators in translational glycobiology possess MD degrees. Indeed, at present, most of the efforts in translational glycobiology are being undertaken by scientists with Ph.D. degrees, essentially all of which have had prescribed preparation for careers in glycoscience. However, the contributing authors for this theme issue were chosen specifically because they are each accomplished clinicians, and, notably, because each did not have formal training in the discipline of glycoscience. Inspired to find solutions for alleviating the suffering of their patients, each clinician

pursued translational research that ultimately converged on glycoscience, yielding new insights in our knowledge of the structure and biology of glycans in human physiology and pathobiology. Importantly, rather than being daunted by the lack of strict training in glycoscience principles and practice, each pressed forward to attain the requisite background knowledge of glycoscience and, where needed, forged collaborations in order to unveil how glycans control the fundamental biological processes that impact the welfare of their patients. Thus, in seeking to unravel the mechanistic basis of the diseases and conditions they treat first-hand, their efforts in "translational glycobiology" have provided transformative strategies to improve clinical practice.

Reference

Bush V. 1945. *Science, the Endless Frontier: A Report to the President (on a Program for Postwar Scientific Research)*. Washington, DC: U.S. Government Printing Office.