Foreword

"Hey Red, catch this?" Looking up, I spotted the grinning face of John Philip Trinkaus as he lobbed a hen's egg whose trajectory promised to land as a yolky splash mess atop a pile of papers on my desk. Happily, I gingerly snatched the egg in mid-air. I could have hurled the egg back to him but, knowing Trink, I knew that he would have dodged it and let it splatter against the wall of my office. Instead I delivered myself of a few remarks that would likely have been bleeped even on today's TV and radio.

What's this thing with eggs? We were budding embryologists, predoctoral students in the laboratory of Professor Benjamin Harrison Willier at The Johns Hopkins University in Baltimore, Maryland. Each of us was engaged in research on problems that were best carried out on embryos of the common domestic fowl.

We first met at Hopkins in 1941, when, as graduate students in the Biology Department, we were assigned as teaching assistants in the Introductory Biology Course. I had flaming auburn hair way back then, so Trink promptly identified me as "Red." Trinkaus was then, and ever since has been, "Trink" to three generations of friends and colleagues. Trink himself was named after a relative, John Philip Sousa, The March King. Generations of school and military bands have marched to Sousa's thrilling beat. But Trink marches to his own beat. And his march has brought him an international coterie of friends and admirers, earning him international recognition as an outstanding scientist among the company of scholars known as embryologists.

The egg-tossing incident was an early event in a friendship that has spanned more than 60 years. I can think of only one scientific colleague, Eugene Copeland, who has known Trinkaus longer than I. So, it is perhaps fitting that I should be asked to provide a *Foreword* to his memoir. This assignment gives me the opportunity to resurrect pleasant memories of our long association, and, it provides a venue for me to reflect on the character of Trinkaus the man and the scientist. Further, it enables me to pay tribute to a cherished colleague whose friendship I hold dear, and to the embryologist whose contributions to our chosen field of research have earned my utmost admiration.

My early encounters with Trink left me greatly in awe of him. When we first met, his educational experiences had already brought him into intellectual contact with many distinguished biologists of whom I had knowledge only from textbooks or from their published papers. In contrast, my education had given me little or no exposure to scientists of national or international reputation. Could I ever hope to be accepted into such distinguished company as Trink had already enjoyed? Indeed, I continue to be somewhat in awe of Trink for, as you will glean from this memoir, he continues to stand as a person to be reckoned with in our science. There is clear witness to his remarkable scholarship, notably in that the National Institutes of Health supported his research well into his years of formal retirement. This support culminated in a National Merit Award that financed nine years of support even as he passed into the late seventies of his life.

Trink and I share many personal and professional experiences, the memories of which are most poignant especially as they relate to our early years at Hopkins. These memories may also provide insights in Trinkaus's character that might otherwise escape the reader. In 1941, for example, my fiancé, Lilyan Clayton, then a graduate student at Duke University, needed a job in Baltimore in order that we could afford married life together. Trink, having multiple contacts through his political activities, nominated her to a friend at the School of Public Health at Hopkins who promptly hired Lil as a research assistant on a project relating to vascular physiology. So, thanks to Trink's help, now we could count on our magnificent combined monthly incomes of $135 to support us while I pursued the doctorate.

As Trink describes, after wartime military service, we both returned to Hopkins to resume graduate study in 1946. Trink meanwhile married his fiancé Galya Ivanovna Gorokhoff. Our families found living quarters in a housing project in east Baltimore called Armistead Gardens. Soon after, Galya gave birth to their first child, Gregor. Lil brought Galya and Gregor home from the hospital in our little Ford coupe, too small to accommodate Trink plus mother and child. Lil, by that time an experienced mother of two, gave Gregor his first home bath. Many years later, at Trink's seventieth birthday celebration at Woods Hole, Lil identified herself to Gregor as the one who taught his mother how to bathe him. Our lives have been intertwined in similar intimate ways since then.

At Hopkins, we shared relationships, albeit somewhat disparate, with our doctoral mentor, Professor B.H. Willier. To many, our mentor came across as stuffy, arrogant, standoffish, uncaring, and unapproachable. This was certainly my initial impression, which Trink shared. That Trink never warmed to Willier is clear from this memoir. Eventually, however, I came to a somewhat more favorable assessment of him. This was thanks to my wife, who, after her first meeting with Willier, assessed him as a shy and somewhat insecure person who was not at ease with his students. With this insight, I was able to establish an informal and moderately comfortable relationship with him.

Regardless of the nature of their personal relationships with Dr. Willier, those of his students who survived the rigors of his training have enjoyed a degree of professional success that has identified them uniquely as Willier's students. Willier sponsored thirty-four doctoral candidates who, by and large, have achieved international recognition as teachers and investigators. They have served as advisers to federal agencies, editors of significant journals, officers of major professional societies, and so on. It is almost certainly true that none of Willer's contemporaries, some otherwise more distinguished embryologists than he, produced as meritorious a generation of students as he did. It is true that, of all of Willier's students, only Trinkaus equaled or surpassed his mentor's record in sponsoring students who have made outstanding contributions to the study of embryonic development. I think that Trink would agree that he benefited greatly from his association with the Willier group even though he and Willier were never close on a personal level. Clearly, Trink had the skill to leverage a less than optimal personal situation into a triumph.

This memoir is aptly entitled *Embryologist*. That is what Trinkaus is: a person who studies the events that lead to the formation of the egg, its activation and division, and the subsequent events that lead to the formation of a functional individual from a single cell, the zygote. The sum total of these events is called development. Development is *progressive*, each step involving the participation of processes and conditions established by antecedent steps. The proper study of development is more than simply the physical description of the progressive morphological changes that take place as development proceeds. The analysis of the various mechanisms that drive these sequential morphological changes is of paramount importance to most experimental embryologists. An experimental embryologist needs to learn what happens and what causes events to happen. The experimental embryologist is legitimately concerned with the multiplication of cells, their movement as single cells and as cellular masses, their organization into multicellular tissues and organs, their individualization as cells of different structure and function, the patterns of gene expression that underlie this progression of events, the physicochemical conditions that elicit or enable these activities, and so on.

Trink's choice has been to focus on two closely related aspects of developmental processes. These are, namely, the movement of individual cells and their integration into morphological patterns, and the mass movement of cells that create the major divisions of the eventual body plan; i.e., the process called *gastrulation*. In this memoir, Trink weaves the story of his contributions to these areas of study into the fabric of his own life story: his loves and families, the politics and problems of academia, and his concerns and responsibilities as a world citizen. His account throughout is imbued with his *joie de vivre*, his loyalty to his friends, and his disdain for pretentiousness and hypocrisy. I trust that you will find these aspects of his story as fascinating as I do. I also hope that you will

gain a full appreciation of the man as a scientist, and that what I have to say will be meaningful in this context.

Understanding the way embryonic cells move, coordinate their activites, and assemble into tissues and organs, has been the center of Trink's life-work. Indeed, his earliest studies, even as an undergraduate, were concerned with motile cells. Among the most motile of cells in the vertebrate embryo are those that arise from that part of the primitive central nervous system called the *neural crest*. Throughout his career, Trink has been concerned to a greater or lesser extent with those derivatives of the neural crest called melanoblasts. These are stem cells that give rise to pigment-producing cells called melanocytes, cells that produce pigment granules that give color to skin, feathers, and hairs, or that aggregate to form colored assemblies. Trink "cut his teeth" in research on problems of the genetic control of pigmentary patterns in a fish. His continuing interest during later years in the role of melanocytes in the realization of pigmentary patterns is amusingly described in his account of the dramatic assembly of migratory melanocytes in the yolk sac of the blennie, a marine fish that he studied in a marine laboratory in Roscoff, France, toward the end of his career.

For his doctoral research, Trink studied the formation of pigment patterns of feathers in the Brown Leghorn fowl. As you read, you can suffer with Trink through the vicissitudes that assailed him throughout this study. Despite some early setbacks, his work was successfully completed. He found that the same line of stem cells give rise to melanocytes that produce either red or black pigment granules. Further, he found that individual melanocytes produce either red or black granules but not both. Finally, he showed that the developmental history of the site to which they migrate and the amount of estrogen available at that site determines whether melanoblasts differentiate into red or black melanocytes. I consider this thesis to be an important piece of work, for it gave new insights into the way in which a cell's chemical and physical environment affects the pattern of its differentiation. Indeed, at Hopkins, it would not have served as a doctoral thesis if it did not contribute significant new knowledge to our understanding of the factors controlling pathways of cellular differentiation.

In the account of these early studies, we find signs of the remarkable powers of observation that have laid the foundation for Trink's subsequent work. One of his greatest pleasures was and still is watching the behavior of cells with the aid of a microscope. As you will find upon reading the memoir, and, as he quotes from Yogi Berra, "You can observe a lot by just watching." Observing cells in their minutest detail, and recording every aspect of their behavior, alone and in contact with other cells, has occupied his interest throughout his remarkable career, which has now included seven decades of the twentieth century and one in the twenty-first century (so far). Moreover, he has shown an outstanding ability to integrate the results of his own work with results revealed

by his critical examination of all aspects of the behavior of cells in development, whether from his own laboratory or from that of others.

The measure of his scholarship can be appreciated from the analysis of almost any of his published papers. He clearly asks penetrating questions about the mechanism whereby cells move, how they interact with their neighbors, and how their movement is affected by the topography of the substrata on which they lie. With critical insight, he recognizes the crux of the problem he is attacking, and mobilizes to its solution the results of his own meticulous observations as well as those of other investigators. As I write, Trink continues to write too, and to ponder his observations of cells, particularly those of his favorite organism, the killifish, *Fundulus heteroclitus*. Significant papers have emerged from his laboratory often since his formal retirement in 1988.

But, one need not review his postdoctoral papers and those of his students to gain an appreciation of the way Trink goes about science. The catholicity of his knowledge about cell behavior and his ability to mobilize it to the solution of important problems is brilliantly attested by his now classic book, *Cells into Organs*, the second edition of which was published in 1984. The value of this work transcends time. This book is truly a *tour de force*. Trink's enduring fame and respect could rest on this accomplishment alone, had he been satisfied to drop his beloved laboratory research after completing this book.

What has fascinated me most in following Trink's research career since we were students is what I like to call the "Saga of Gastrulation." This is a story of epic proportions, developed over many years, that reveals the mechanisms whereby the embryonic body of the fish emerges from the fertilized egg. The zygote of *Fundulus* begins its development as a single cell, like a protoplasmic bump containing the zygotic nucleus sitting atop a round mass of yolk. The membrane that covers both the yolk and the nucleated cell is continuous. Cleavage of the cell does not divide the yolk, but gives rise to a population of cells over the yolk as the embryonic body emerges. Analysis of the mechanisms whereby the blastoderm envelops the yolk has involved microsurgical manipulation, light and electron microscopy, electrophysiology, techniques for measuring forces exerted by embryonic cells, and the application of results gained from many observations of cellular behavior from his own and other laboratories. In this memoir, you will find insights into the way in which Trink and his co-workers identified the problems of gastrulation and the clever ways they devised to solve them.

Trink writes eloquently and at some length of his study of gastrulation, so I shall comment only on two aspects of his work that I find particularly perceptive and exciting. The first of these is the identification of the yolk body as a syncytial cell, appropriately called the yolk cell, the multinucleated portion of this large cell underlies the cellular blastoderm and precedes the advancing edge of the blastoderm in gastrulation. The second of these is the discovery that

endocytosis diminishes the yolk cytoplasmic layer in advance of the blastodermal margin during epiboly. Endocytosis is an unusual and fascinating morphogenetic mechanism. Trink and his co-workers analyzed this mechanism in meticulous detail utilizing modern imaging techniques.

Trink's claim to recognition as a scientist is further supported by the role he played as mentor of generations of outstanding teachers, investigators, and scientific administrators. Indeed, replies from all of whom I have inquired, by and large emphasize Trink as mentor and exemplar of devotion to scientific rigor. This role, combined with outstanding teaching and writing, will provide enduring inspiration to students for generations to come. My discussions with Trink reveal that he regards his greatest contribution to science to be his performance as a teacher and an inspiration to future generations of developmental biologists. The loyalty, respect, and gratitude of his students, undergraduates, doctoral candidates, and postdoctoral associates was dramatically revealed at the "Trinkfest," held at the Marine Biological Laboratory in Woods Hole, in honor of his seventieth birthday. Organized by former students and friends, it attracted an international group of celebrants, from the working scientific community, plus a large number of former undergraduate students, who gave outstanding tribute to Trink as an inspiring teacher and advisor.

Before we canonize Trinkaus to some kind of scientific and pedagogical "sainthood," it is probably appropriate to recognize that there are some, not many, to be sure, who have less than complete admiration of him as a person and as a scientist. There are those who would condemn him for some unconventional aspects of his life style, particularly from his younger years. For his way of life, Trink makes no apologies, nor does he need to. He is an honest man! There are those, too, who take offense at his outspoken judgments of others that he thinks are being less than honest in their own self-evaluations. Too, there are those who are the recipients of adverse criticisms of their scientific work. Trink is, like the rest of us, sometimes wrong in his judgments, but he makes them honestly and in the interest of "having it all out on the table" for all to see. Trink has a compulsion to expose what he judges as error, what he sees as pretentiousness, and cant. Some would want him to be more diplomatic in expressing his evaluations of others, both in their science and personal lives. Diplomacy has not generally been Trink's way. Where science is concerned, however, thoughtful criticism, however seemingly harsh, should be evaluated honestly and not be perceived as a personal attack; rather, as a method for establishing the truth.

As one looks over Trink's career, as revealed in this memoir, it is clear that he has had a life that many might envy. When you read of his experience as Master of Branford College, and the many perquisites attending this position, you might ask, "Why couldn't I have had such an opportunity?" You might wish, too, that you had been rewarded with as many opportunities to travel and to meet

and interact with an international coterie of scientists and notable public figures such as Trink has enjoyed. The fact is that Trink worked hard and planned well to gain these opportunities, enjoying life all the while. Envy, if it exists, should be replaced with admiration.

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