



Why wait for posterity (or the future) to provide proof to savor the elixir of precision oncology? Read interviews with intellectuals and dine with the doyens of discovery

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It is sad that as we seem to advance further into the ever-increasingly complex realms of science and medicine our strategies appear to become more naive and simplistic. To some extent, this reflects the digitalization of information and the quantification of thought rather than an expected inspiration of the quintessence of comprehension and assessment. Somewhat regrettably, therefore, it seems that the evolution of thought in the last decades has shifted further and further toward the concept of binary responses (yes or no) with respect to monodimensional questions (therapy works or not, or lesions exist or not?). How we have lost comprehension of the vast spectrum that is represented by the ceaseless and amaranthine interaction of disease and the unique cellular and chemical and genomic matrix that is ourself. This disturbing vision provides a consequence that directly involves nuclear medicine as oncology has more and more become the province of “moonshots” and “Hail Mary” passes. These frequently speculative and more-often hyped concepts are disproportionately driven by the marketing decisions of “big pharma,” vogue (fake news) assessments of worth rather than by the scientifically based concepts of logic, ideation, creativity, and genius. The medical and scientific surrogates of Galileo, Copernicus, Kepler, Leeuwenhoek, and Spinoza are rarely found as politics, power, and speculation have

devalued the spirit of novel, medical, and scientific creative and inspired thought.

As a consequence, tumor cells must find it risible when seeking to assess the intelligence of *Homo sapiens* and their paltry efforts to alter survival ratios using sticks and stones (monotherapy and its random permutations and commutations) to confront the millions of years of embedded molecular biology designed to ensure neoplastic cell survival. How primitive to address the unimaginable and as yet mostly uncharted complexities of cell growth and survival by continuing to use the technical, biological, and pharmacological equivalents of a hammer and a “less than sharp” stone. Even more intellectually disturbing is the naive notion that during the entire sequence of therapy options, tumor cells remain static and with immutable defenses: a consideration as flawed as the archaic concept of the fixed Maginot Line being an effective protectant. Few seem able to integrate into their therapeutic concept the well-demonstrated biological reality that neoplastic cells continually evolve in their search for survival and proliferation. Thus, any therapeutic strategy has to comprise real-time delineation of the machinery of the destructive cell as well as a molecular assessment of ongoing neoplastic chimerization as the cell seeks to outflank its administered agents of destruction. The concept of the cancer cell as a medieval citadel being attacked by an army with ballistas is as outmoded as the Hippocratic notion that cautery might cure cancer. We seem to have forgotten the cunning of Ulysses and the magic of Circe and remain fixated upon scorched earth policies and firepower as opposed to the Byzantine strategies of success espoused by MI5 or the Mossad. We have embraced chemical blitzkrieg rather than Machiavelli and diplomacy as our models and consider success as failure to die (irrespective of cost and adverse events) rather than life quality as our lodestone.

Rather than continue the almost-futile reiteration of past strategies, there is a pressing need to embrace and introduce

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novel technologies and conceptual advances. This should be undertaken on many fronts rather than a single file strategy by developing and interfacing a broad array of innovative ideas. Thus, the introduction of new imaging techniques (functional and topographic), multigenomic molecular biomarkers (that define cell behavior and treatment efficacy in real time), and providing a continuum of information on the neoplasm's activity rather than delayed snapshots are needed. Above all, the mathematical integration of such information using artificial intelligence to quantify and predict as opposed to opinion-based interpretive debate (multidisciplinary droning) is a mandatory component to advance. The muttering mavens of mediocrity and the nattering nabobs of nihilism must be replaced by a new generation of Galileos, Hunters, Cricks, and Lauterburs. A mathematical matrix of a patient's disease combining not only the image and molecular determinants of disease status but also the individual theranostic, pharmacokinetic, and pharmacodynamic parameters of the individual needs to be developed. Contrary to the thoughts of the sixteenth century metaphysical poet John Donne (no man is an island), indeed in terms of the molecular and cellular basis of neoplasia, "each man is an island" and his particular tumor unique. One might as well make one garment for all persons and imagine a perfect fit, as conceive a common treatment strategy effective for all tumors of a specific semantic categorization.

So how disappointing is it to note that nuclear medicine as one of the first of the medical disciplines to embrace the integration of cell physiology, molecular targeting imaging, and therapy (theranostics) has lapsed into reiterative development rather than embrace "beyond the horizon" strategy development. Rather than have radiolabeled probe theranostics provide monodimensional information, there is the need to incorporate diverse molecular information. This should provide a cornucopia of knowledge of multidimensional tumor cell- and milieu-specific elements that can be integrated to produce a real-time patient-/disease-specific portfolio. With such information, delineation of the molecular pathobiology can be assimilated into providing a complex *patient-specific disease model*. Three-dimensional tumor topography integrated with functional molecular genomic quantification using mathematical modeling and system biology analysis can allow nuclear medicine to provide a roadmap to precision oncology, in essence providing the input basis for a GPS system that could provide the basis for predictive therapeutic guidance and assessment.

Lest such a proposal seem utopian or even reflective of intellectual hubris, we ask you to bear in mind the thoughts of Albert Einstein in *Ideas and Opinions*. [1]

But before mankind could be ripe for a science which takes in the whole of reality, a second fundamental truth was needed, which only became common property among philosophers with the advent of Kepler and

Galileo. Pure logical thinking cannot yield us any knowledge of the empirical world; all knowledge of reality starts from experience and ends in it. Propositions arrived at by purely logical means are completely empty as regards reality. Because Galileo saw this, and particularly because he drummed it into the scientific world, he is the father of modern physics—indeed, of modern science altogether.

Unarguably one of the great intelligences of the ages and certainly a thinker not averse to the prediction of the unthinkable, Einstein's words provide a clear guide for the nuclear medicine scientists. While logical thinking, empirical data, *p*-values, proofs of principle, and linear thought all are based on knowledge, they all have "experience" at the very core of their hypothesis. Such experience can best be appreciated and learned from by understanding how the development of the hypothesis (like the complex enrichment of isotopes) was undertaken. We propose that the understanding, appreciation, and incorporation of such thought into practice can be facilitated by enquiry of such intellectual pioneers as to the logical steps that led them to their vision of new scientific horizons and its application to the advance of knowledge. Let us learn from them now—not tomorrow. As noted by George Stewart, we should listen and reflect so that we may better understand.

Here, the distilled wisdom of the years,
The slow deposit of knowledge gained and writ
By weak yet valorous men who shirked not the difficult
emprize
Unshared must be their genius, It was their own
But you, be you brave and diligent, May freely take and
know
The rich companionship of others' ordered thought [2].

This is one of the reasons EJNMMI has decided to open a special section on interviews with pioneers and stalwarts of the advance of medicine and science. These interviews are primarily aimed at the present and next-generation scientists and clinicians to learn from the experiences of people who have contributed significantly to the field of nuclear medicine or fields that have facilitated the advance of the discipline. Apart from publishing interviews of nuclear medicine fraternities, EJNMMI seeks to provide exposure to non-nuclear medicine disciplines (e.g., pathologist, surgeons, oncologists, gastroenterologists, endocrinologists, radiation oncologists, urologists). It is our belief that their experiences will be equally valuable in providing the elixir that resides within the framework of precision medicine and precision oncology.

We trust you will be inspired by their intellects and delight in their deliberations as we all move toward greater understanding and the attainment of the ultimate Hippocratic horizon of health.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical statement This article does not contain any studies with human participants or animals performed by any of the authors. All statements represent the sole personal views of the authors and are independent of the institutions they are associated with.

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1. Einstein A. Ideas and opinions. NYC: Crown Publishers; 1954.
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