Translational Medicine

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Is There A Natural Translational System Suitable for the Target Therapy of Lung Cancer?

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Commentary

Merriam–Webster's Collegiate Dictionary recently defined "translational" research, a word first used in 1986, as "medical research that is concerned with facilitating the practical application of scientific discoveries to the development and implementation of new ways to prevent, diagnose, and treat disease" [1].

In this context, it is apposite to mention that, a century earlier, Cohnheim [2], the great German pathologist, emphasized that autopsy findings "are all in a manner experiments instituted by nature, which we need only rightly interpret to get a clear idea of the causes, laws of growth, and significance of the tumour."

Nearer in time was the 1926 expansive explanation by Nicholson [3] as follows: "We pathologists can dispense largely with experiments, since nature has done them for us upon a much grander scale than is possible for the boldest experimentalist. We have unbounded opportunities for studying the effects on the body of every conceivable alteration of the environment."

Hitherto, autopsy practice had been such that the body parts were cut up and displayed separately on the dissecting table. On my part [4] to obtain a better panorama, I introduced the "mono–block formalin–fixation method for investigating cancer metastasis."

A good outcome of this practice was the discovery that, on tracing the earliest cancer deposits lying in centrifugal order among the abdominal lymph nodes, a curious pattern materialized [5]. Significantly, the deposits were not found in the retrograde position, i.e., the hilum, or the concavity but in their convexity. Therefore, I argued convincingly many times as follows:

- "newly formed afferent vessels".
- "New afferents open up."
- "Newly-opened backwardly-directed lymphatics."
- "New retrogradely-directed afferent lymphatics."
- "new afferent lymphatics links."
- "Probably most often transported backwards by way of newly formed afferent lymph Vessels."
- "Such afferents effect connections."

Thus, as I showed elsewhere [6], these findings were of the order of "Premature Discovery." Little wonder that, nowadays, the phenomenon goes by the appropriate name of lymph angiogenesis. Furthermore, it has been identified for target therapy purposes [7,8], Incidentally, I have published that this phenomenon explains the longlasting puzzle concerning the selectivity of the adrenal glands during the metastasis of lung cancers .

As far back as 1798, the great Sir Astley Cooper [9] had recognized the importance of "the thoracic duct in the human economy." Hitherto, the problem was the difficulty that this 45 cm long organ presented to researchers. It had to be cut and examined as numerous microscope cross sections [10]. However, on my part, I devised the Swiss-roll method of coiling it and properly processing it so as to examine it with a single microscope slide [5]. This maneuver revealed the panorama of lung cancer cells being transported through this special conduit at the moment of death.

Most importantly, there was the following concrete conclusion:

"Necrosis of the cancer cells was apparent in 3 cases, but it was clear that this had occurred in association with large aggregates of the malignant cells and that among such aggregated cells red blood corpuscles abounded."

It was necessary to argue that this was an important observation. The following were the germane grounds:

Firstly, according to the 1955 Harveian Orator, Melville Arnott [11], it is necessary to follow up any anomalous finding because it may lead to an advance in science.

Secondly, I advanced as many as seven such anomalies pertaining to lung cancer metastases [12],

Thirdly, any oddity observed on studying lung cancer spread deserves particular attention.

Therefore, the above observation on the necrosis of lung cancer cells, when associated with erythrocytes in the lymphatic microenvironment of the thoracic duct deserves profound attention. So far, I have suggested that a hidden factor must be present. I even named it "The Erythrocyte, Associated Necrosis Factor" (EANF). I added that new investigations should be undertaken. Here, it suffices to stress that the commonly employed cannulation [13] of the thoracic duct can be employed in consenting lung cancer patients so as to retrieve for study the two available subsets of both necrotic and lively cancer cells with the new technique of intravital video microscopy [14].

Conclusively, I suggested that leading laboratories should undertake the replication of the materials accruing from these maneuvers. Fortunately, Steven Woolf [15] documented both the meaning of translational research and why it matters. In his words, "The National Institutes of Health (NIH) has made translational research a priority, forming centers of translational research at its institutes and launching the Clinical and Translational Science Award (CTSA) program in 2006." As he continued, "By 2012, the NIH expects to fund 60 such centers with a budget of $500 million per year."

So far, the U.S. Food and Drug Administration (FDA) has approved afatinib tablets, after successful experimental work, for the treatment of lung cancer [16] Indeed, the NIH, on its part, has "translational medicine" as a major focus [17]. The National Cancer Institute (NIH) has cosponsored conferences. One report [18] was on using Combretastatin A-4 Phosphate on a single-dose intravenous schedule in patients with advanced cancer. It instanced the following: "A patient with anaplastic thyroid cancer had a complete response and is alive 30 months after treatment." There is also the NCI pilot project for acceleration of translational research [19]. The report was positive thus: "These findings reflect the current status of the cancer vaccine field, highlight the possibility that additional organized efforts and funding would accelerate the development of therapeutically effective cancer vaccines, and accentuate the need for prioritization" [20].

Be that as it may, I would suggest that it is this emerging translational system that will soon facilitate breakthroughs. However, in all probability, focusing comparatively on how Nature already handles this enigma from the angle of EANF may pay the hitherto largely elusive paramount dividend. Indeed, this eventuality will be more than hastened by the combination of both basic and clinical translational researches [20].

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