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The Role of Pathology in Personalized Medicine

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The post Human Genome Project explosion of applications of genomics, proteomics, and bioinformatics is rapidly changing the way clinical and experimental pathology is conducted. We hope this journal will attract manuscripts about the latest discoveries and the most innovative approaches to understanding human diseases, creating a forum for dialogue and debate. This journal, being of the open access type, will allow free access to full text articles. At the same time authors will also gain better exposure of their published work to a wide audience of a million readers.

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As all nations struggle with sustainability of their healthcare systems due to rising costs and the increasing prevalence of chronic diseases including cancer, we have to become more evidence-based in our practice. We need to move from the tyranny of "one size fits all" paradigm to evidence-based and thoughtfully designed personalized medicine. We must remove waste from our systems so that resources are better allocated to where the needs are. This is difficult to do as medicine tends to be tradition driven, new knowledge takes time to become mainstream, and we are often trapped in the rituals of practice considered to be the standard of care even though outcomes are not satisfactory.

In a recent review article [1] I examined the cost of the current cancer management approaches in Canada, which has a publicly funded healthcare system. Of the OECD countries, Canada has the second highest per capita spending on drugs (second only to USA), and total spending on drugs reached over $30 billion a year in 2010, representing over 16% of total healthcare expenditures (https://secure.cihi.ca/estore/productFamily.htm?pf=PFC1615&lang=en&media=0). In the cancer care field, this problem is compounded by the fact that 75% of cancer therapies do not benefit patients [2]. The cost of treating Canadian cancer patients with ineffective protocols was calculated to be in the range of $1.2 billion per year [1]. I suspect similar waste occurs in the management of other chronic illnesses such as type II diabetes, cardiovascular disease, various mental illnesses such as clinical depression, and so on.

I believe pathologists and other laboratory physicians and scientists can make a difference. Discoveries of previously unknown genetic defects in specific disease entities are beginning to be published through combined efforts of pathologists and genomics experts. Recent examples from the British Columbia Cancer Agency (BCCA) Centre for Lymphoma Research include recurrent somatic mutations in follicular and diffuse large B cell lymphoma affecting the polycomb-group oncogene EZH2, which encodes a histone methyltransferase responsible for trimethylating Lys27 of histone H3 (H3K27) [3], and somatic mutations in MLL2, which encodes a histone methyltransferase, in a third of diffuse large B cell lymphoma and 89% of follicular lymphomas [4]. Examples of genomic discoveries in other cancers at BCCA include ovarian cancers [5,6], and mapping pathways responsible for drug resistance in an individual patient [7].

What has led to this fruitful collaboration? First, British Columbia has a province-wide cancer control system, hence there is a high degree of standardized evidence based practice which is the result of rapid application of new discoveries to a population-based cancer control system. Second, high quality cancer care and research have been investments made by the leaders of BCCA who perceived that these are synergistic activities as one drives the other bidirectionally. Decades of effort into tissue banking, the existence of linked pathology, genetics and clinical outcomes databases which have been in place for over 20 years, and the creation of the largest high throughput gene sequencing centre in a cancer hospital, the Michael Smith Genome Sciences Centre, incorporating next generation sequencing technology, have come together in a powerful way to allow rapid discovery of genetic abnormalities in lymphoma samples. Each of these discoveries has the potential to spin-off novel targeted therapies, allowing a more personalized approach to lymphoma therapy. This model can also work for other cancers and, indeed, other chronic illnesses.

The future for pathology to lead in designing rational therapies is great, but we need to step up to the plate. There is a risk that this potential will be lost if bean counters, aka hospital administrators and healthcare funding bodies who look at pathology as a commodity that can be squeezed in order to free up funds for clinical care, are allowed to make uninformed cuts in laboratory budgets and infrastructure. That would guarantee the perpetuation of the wasteful paradigm in which we currently practice.

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