Do We Know Enough to Develop Precision Medicines?

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Introduction

“Precision medicine” has been defined as “medical care designed to optimize efficiency or therapeutic benefit for particular groups of patients, especially by using genetic or molecular profiling”. Do we have enough knowledge to do this in an “intelligent” manner?

Several authors have now questioned the rationale, sensibility, and likelihood of success of the “precision medicine” idea as it is currently being envisioned. Efforts to develop personalized disease treatment based on the DNA of individuals have not been successful. Even the suitability of the term “precision medicine” has been questioned in Uncertainty in the Era of Precision Medicine. National Research Council explained that the word ‘precision’ is being used to mean both ‘accurate’ and ‘precise’. The word “precision” implies that the intended outcome, result, will be delivered with a high degree of certainty. Do we know enough about the function of human genes to do that?

It is hard to justify the current rationale for developing disease treatment based on understanding of human genetic code. After all, only the part of the genome related to expression of proteins have been studied; our understanding of this part of genome is far from being complete. Further, the part of genome relevant to this represent only some 1 to 2% of the total code. It is unlikely that the rest of the genome has no biological function.

It is indeed hard to understand how complex molecules of human genome could indeed develop via a random process, given its overall size being stated as 6 billion of DNA base pairs. The scale of this happening by a random process over time is hard to grasp. Few years ago, Mr. Bob Newhart popularized in a comedy sketch a likely time-line needed. I paraphrase: “A group of monkeys, typing by hitting keyboards at random over an infinite length of time would reproduce the Complete Works of William Shakespeare.”

Interestingly enough, Dr. Ian Stewart (an emeritus Professor of Mathematics, University of Warwick) suggested that for monkeys randomly to recreate, in the right order, the 3,695,990 characters of Shakespeare’s work would take some 13 to 14 billion years (i.e., about the same time as the current estimate of the age of the universe). In comparison, reading the whole human genetic code at a speed of one base pair per second would take a person some 190 years.

Many years before we learned anything about the DNA and genes, Mr. Charles Darwin speculated on the origin of life saying that “the intimate relationship between the vital phenomena with chemistry and its laws makes the idea of spontaneous generation conceivable,” however at the same time he recognized that “... science was not advanced enough to deal with the question and that he would not live to see it resolved.” Given Mr. Darwin’s upbringing it is not surprising that he referred to a Creator of life in his earlier work On the Origin of Species. By the same measure, it is not surprising that later, when he started to understand the complexities of natural life and its continuing development, he regretted using the Pentateuchal term of creation, by which, as he wrote later “...really meant ‘appeared’ by some wholly unknown process” (sic). On a separate occasion, Mr. Darwin made his position even clearer: “It is mere rubbish, thinking at present of the origin of life; one might as well think of the origin of matter”.

On balance, I feel it is probably more likely that such complexity has developed by a “random process” over a very long time rather than by an “intelligent design”. The process of evolution in itself is not easy to rationalize, from human perspective. For example, how could a snake develop its venom? What would be a random process without an “intelligent” input. No matter how one looks at it, there are many question that cannot be answered.

At present, very little is known about functions of genes as it relates to disease. To date, the focus has been on genes that code for proteins; it is not likely that the remaining 98-99% of human
The genome has no biological function... Little, or an incomplete knowledge could be a dangerous tool to have.

Discussions and planning of Precision Medicine activities have not addressed in detail how the knowledge gathered by the initiative will be used to treat patients. Will there be genes identified that are responsible for a disease development or progression; or will there be genes which when absent might be the cause of disease? Will treatments focus on changing, adding or replacing genes? Will genetic information provide specific information on disease targets to address? Will the information be used to design and develop new drugs? If so, it could be expected that the "precision" of this development will require a precise manner in which these new drugs will need to be used.

All these requirements will need to be set against the current "state of the art" which does not enable site-specific delivery of existing drugs. A call for changing the paradigm for site-specific drug-delivery research has been made, and should be responded to [7].

References