Set Theory: A New Way For Looking Liver Cancer Development, Progression And Metastasis

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Abstract

Despite advances in our genomic and cellular knowledge, hepatocellular carcinoma (HCC) remains one of the major public health problems throughout the world. HCC still represents the sixth common cancer worldwide, it is the most common primary cancer associated with hepatitis B and hepatitis C virus chronic infections, alcohol abuse or in developing countries with food contaminated with *Aspergillus flavus* fungus. HCC is now recognized to be highly heterogeneous: it encompasses a wide range of clinical behaviours, and is underpinned by a complex array of gene alterations that affect *molecular*, *cellular* and *supra-cellular* processes operating at various spatial and temporal scales. It is still widely debated as to how HCC progress through carcinogenesis and acquire its metastatic ability.

Several genomic alterations have been identified in fully developed HCC and to a lesser extent in morphologically defined pre-neoplastic lesions. Although the importance of these data, they have still not led to a complete understanding of the complex mechanisms underlying HCC development, progression and metastasis, or to the identification of key alterations that improve the carefulness of diagnosis or therapeutic interventions.

In simple mathematical terms, HCC can be delineated as a dynamical disease that emerges from a number of alterations that induce changes in expression patterns of genes and proteins that function in complex networks controlling critical cellular events. Analysis of the development, progression and metastasis of cancer cells from natural hepatocytes, and the heterogeneity of a liver cancer cell population raises three main questions:

- what are the properties shared by cancer and natural hepatocytes?
- to what extent are these properties shared?
- why a small number of cancer cells acquire the metastatic potentiality?

Both natural hepatocytes and their tumoural counterparts can be seen as *sets* of different sub-cellular structural entities organized in such a way as to perform all of the functions involved in the *self-maintenance* of cell processes and the functions necessary to guarantee the *cell's existence* and *evolutionary progress*.

Here, we discuss the HCC development, progression and metastasis using the fundamentals of Set theory. Additionally, some of the critical concepts necessary to give meaning to its underlying physical complexity are introduced. This way of looking HCC may help to clarify concepts, indicate alternative experiments and categorize the actual knowledge.