

Signal Transduction Pathways in the Clinical Approach: Where are we Going? **V R Lo Vasco**

Received: November 03, 2015; **Accepted:** November 18, 2015; **Published:** December 05, 2015

Within a cell or a tissue, molecules' production, catabolism, renewal and turnover rate are strictly controlled by complex mechanisms. In the last thirty years, modern molecular biology approaches revolutionized genes and proteins characterization, with the most relevant improvement for low expressed molecules.

The signal transduction pathways are actively studied in an enormous number of human diseases, including cancer and degenerative illnesses. Each human disease might be seen as a "signaling disease". Unfortunately, the causative role in diseases' aetiopathogenesis was demonstrated for a few signal transduction molecules. Signal transduction pathways acting within a cell overlap. For almost diseases it is not clear the impact of a single pathway disruption upon the clinical outcome. Indubitably recent knowledge advances in signal transduction pathways cascades contribute to elucidate the natural history of diseases, with special regard to tumours. Consequently, more than considering a single molecule, it might be useful to evaluate all the related components of the pathway that molecule belongs to. Beside the contribute to knowledge, identification of one or more signal transduction pathways alteration in a disease widens the number of potential targets. When a single gene is mutated causing the disease, studying the molecules which normally would interact with the lacking/abnormal protein might allow correct the abnormality in the signaling cascade. That might multiply the number of elements for diagnosis, prognosis and of targets for therapy. All the molecules belonging to a disrupted pathway or to a pathway related to an altered gene/protein can be considered. That virtually amplifies the number of target molecules (genes, mRNAs and proteins) to upstream and/or downstream, short and/or long distance interacting proteins.

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Another suggestion of the "signaling disease approach" is that the same pathway alteration underlies or contributes to clinically different diseases. As other signaling systems, inositol phospholipids' (PI) pathway acts in many functions, so that its alteration was involved in diseases which differ for aetiopathogenesis and/or clinical epiphenomena, depending on brief/long distance interacting and down/upstream related molecules. PI related Phospholipase C (PLC) enzymes were indicated to be involved in inflammation, tumours, neuropsychiatric disorders and single gene diseases. Recent evidences indicated that PI-PLC findings can add data about the natural history of a disease and clinical outcome. However, more investigations will be required in order to purpose them as diagnostic or prognostic indicators.

Interestingly, PI-PLC enzymes, such as many other signaling molecules, can be efficiently blocked by specific inhibitors, that might indirectly affect the activity of further related molecules. Moreover, recent gene silencing-based reports suggested new possibilities to regulate the expression of PLC enzymes. Although we are far from using our growing knowledge in the field of "signaling diseases" for therapy, that also represents a promising perspective.