

JOINT EVENT ON

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Endogenous toxins as disease initiating events: a new paradigm shift**Subrahmanyam Vangala**

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Disease diagnosis and therapy involves pathological observations, identification of underlying target(s) and developing novel drugs to treat the diseases. This "Target based Medicine" therapy has been popular for the last three decades; however, we still have more than 80% failures in phase III trials resulting in billions of dollars of futile investments into drug discovery and development research. One reason why many drugs fail to work during targeted therapy is the target selection in late stages of diseases is flawed. Many targets are non-specific and non-selective for the underlying disease and confronted with many other redundant and cross-talk pathways making the targets more "casual" than 'causal' of the disease process. In this presentation, a new paradigm is presented where identification of targets in early disease initiation process is critical for successfully preventing the progression of the disease. Accumulation of "Endogenous Metabolites" have long been shown to initiate the injury and ensues cascade of events in cellular degeneration and eventually result in disease progression to an irreversible pathological state. Several examples from "In born errors of metabolism" have documented where a deficiency of one enzyme or protein results in accumulation of "Endogenous Metabolites (Endogenous Toxins)" resulting in disease initiation processes and progressively cause cellular degeneration process. Thus, systematic metabolomic investigations from early childhood can help identify changes in the metabolomic signatures and identify early disease initiating events. A prophylactic intervention at such early stages of disease initiation process can prevent further successive cellular degeneration to incurable pathologic manifestations.