## Kinases: The Heroes without Capes in Cancer Research

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Tr. Sourabh Soni, Ph.D. Scholar from CSIR-Institute of Himalayan Bioresource Technology, Palampur, is pursuing his research on "Elucidating the Role of Mapkapk2 as a Potential Anticancer Target in the Pathogenesis of Head and Neck Squamous Cell Carcinoma." His popular science story entitled "Kinases: the Heroes without Capes in Cancer Research" has been selected for AWSAR Award.

I was born in the lush green surroundings of Palampur, a small hill town located at the foot of the Himalayas. Born and raised in a place with the diversity of flora and fauna at its best, nature always caught my attention ever since I was a little boy. My intrinsic curiosity about nature, a reflective thought process and tacit questioning of things happening around me, moulded me into a relentless learner. I continually have been inquisitive about the latest advancements in science and technology. "Research is to see what everybody else has seen, and to think what nobody else has thought", this stimulating definition of research by Neil Armstrong captured my imagination in high school and has since incited and kept alive my passion to pursue a career in research. Experiencing real research during my doctoral studies has been nothing short of a roller-coaster ride and has provided me with a complete spectrum of excitement, intrigue, realization, despair, relief and tremendous satisfaction!

Now coming to the real question, 'Why did I choose cancer biology as my field of research?' To answer this inevitable query, let me tell you that right from my childhood, I had heard many

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stories and seen many people suffering from ailments that have led to their personal and family lives go haywire. This certainly gave me a push to comprehend and try to learn as deeply as possible about the various causes underlying dreadful diseases like cancer so that I could contribute fundamentally to the field of cancer biology and could be of importance to the society at large. The advantage of advanced learning and exploration is always the adventure and the thrill of venturing into the twilight zones of our intellect and the existing physical world around us. The quest for the unknown and the prospect of becoming the first to unravel a mystery that can have far-reaching effects on countless lives has always intrigued me and given me the stimuli to learn and master new things in life. With this mindset and a desire to learn and gain intellectually, in my doctoral work, I have been working on the topic entitled, "Elucidating the role of MAPKAPK2 (MK2) as a potential anticancer target in the pathogenesis of head and neck squamous cell carcinoma (HNSCC)". The title may look complex at first look but has a lot of meaning and significance if you ask me. Let me try to put it down into a simpler story so that its real relevance comes into the picture.

Life is defined by the regulations of its components in a variety of manner which includes the regulation in gene expression patterns too. Depending on the environmental cues and a plethora of stress factors, the cells in our body respond accordingly. The characteristics of a cell are the reflection of its corresponding genes being expressed and regulated at that moment of time. This holds true both in physiology and pathology. The patterns of gene responses and their interplay with other cellular processes hold the key for the better understanding of both normal cellular behaviour and its alterations during diseases like cancer. Cancer, one of the most dreaded diseases, is quite intricately dependent upon gene regulation with kinases (like MK2) playing the central role. In response to diverse extracellular stimuli, MK2 influences crucial signaling events and cellular processes. MK2 regulates important cellular phenomenon, yet surprisingly the biological significance of MK2 in tumour progression has not been well elucidated till date.

During my doctoral work, I was interested in exploring the area of regulatory molecular biology with the perspective of HNSCC in my mind that is one of the most prevalent in this region as well as nationally. I tried to delve deeper into this area so that I can make an original and significant contribution towards understanding the basic molecular biology in order to better understand this disease process.

In India, around 77,000 cases of HNSCCs are diagnosed every year making it the second most common cancer in the subcontinent. The primary causes of HNSCC are various environmental and lifestyle risk factors including sustained tobacco exposure and alcohol consumption. Owing to the steep rise in HNSCC incidences and associated mortalities, it is not at all surprising that monitoring and controlling of HNSCC is becoming a national priority. Despite advances in surgical and other conventional treatment strategies in recent years, HNSCC continues to have a dismal prognosis with 30-47% recurrence rate as well as quite low 5-year survival rate among all the cancers. Unfortunately, to date, selection of medication in HNSCC has not been influenced by molecular testing/targeted therapy. The limited understanding of disease progression and carcinogenesis of HNSCC has posed huge challenges for the development of new therapeutic strategies. Hence, there is an urgent need to define the mechanistic role of different factors involved

in HNSCC progression. In this context, we examined the involvement of MK2 in the regulation of HNSCC pathogenesis-linked genes by analysing tissue samples from cancer patients, generating MK2-knockdown tumour cell lines and developing xenograft mice model. Through our in-depth experimental approach and analysis, we have finally reported for the very first time that MK2 is a critical regulator of HNSCC progression as it regulates the transcript stability of important genes that showcase important roles in tumour pathogenesis. In a nutshell, we have portrayed a critical role of MK2 in modulating HNSCC pathogenesis and have implicated MK2 as a prominent tumour marker in an attempt to unveil it as a potential novel anticancer therapeutic target in the management of HNSCC. I could write the tough-to-swallow gene names, the fold-changes, the expression patterns and the behaviour of the xenografted mice but that would just complicate the things a bit too much. Hence, I am not going into the technical details and in-depth data and experimental discussions because, at the end, what really matters is the outcome and the benefit that society would reap *via* your findings.

A better understanding of the role of MK2 in tumour progression could provide new insights into the enigma of gene regulation in cancer. HNSCCs are quite challenging to control due to their heterogeneity and demand for improved cosmetic results. Scientific advances in the area of molecular oncology have opened novel research directions. Nowadays, numerous research endeavours have been concentrated towards developing targeted therapies and unveiling novel stage-specific molecular markers which could be utilised in predictions of treatment outcome or in personalised therapies. It is quite evident that further unravelling the molecular tumorigenesis enigma will eventually pave way for novel therapies and better tailoring of present treatment modalities for the patients. Hence, our findings which are the hard-earned fruits of continuous and untiring efforts, can contribute significantly to the understanding of inhibiting malignant development and leading to a better disease-free life for the patients. This could serve to be a boon for the society which has been constantly plagued by this horrendous ailment.

This brings me to put a close on the story of my research for now. At this crucial juncture in my career where I am about to launch myself into an independent researcher, I look back with content at my findings and just hope with fingers-crossed that all the countless lab-hours were worth-it-all. It would be really heart-warming and overwhelming to see my research be of clinical and societal benefits in the days to come. I hope that I was able to communicate the intricacies and the earnest importance of the study in a simple way and put forward a probable answer to the million dollar question, "How can we control and treat cancers?"