I am a physician scientist trained in pathology and cancer biology. My lab has made a series of discoveries published in Nature, Science, and Nature Genetics, that have identified a central role for ecDNA (extrachromosomal DNA) in cancer development, progression, accelerated tumor evolution and drug resistance. These findings have provided a new understanding of the fundamental mechanisms of oncogene amplification and the spatial organization of altered tumor genomes, launching a new area of cancer research that links circular architecture with tumor pathogenesis. I lead Team eDyNAmiC, which was awarded one of the $25M Cancer Grand Challenges Awards from CRUK and the National Cancer Institute, to tackle the extrachromosomal DNA grand challenge. My lab has also uncovered metabolic co-dependencies that are downstream consequences of oncogene amplification. These include a central role for altered biochemical mechanisms that regulate oncogene copy number and function. These discoveries have resulted in new understandings of some of the fundamental processes by which oncogene amplification drives cancer progression and drug resistance and pointed that way towards new treatments that are being developed.
CURRENT RESEARCH AND SCHOLARLY INTERESTS

Human genes are arranged on 23 pairs of chromosomes, but in cancer, tumour-promoting genes can free themselves from chromosomes and relocate to circular,
extrachromosomal pieces of DNA (ecDNA). These ecDNA don’t follow the normal “rules” of chromosomal inheritance, enabling tumours to achieve far higher levels
of cancer-causing oncogenes than would otherwise be possible, and licensing cancers with a way to evolve and change their genomes to evade treatments, at rates that
would be unthinkable for human cells. The altered circular architecture of ecDNAs also changes the way that the cancer-causing genes are regulated and expressed,
further contributing to aggressive tumor growth. These unique features make ecDNA-containing cancers especially aggressive and difficult to treat and cancer patients
whose tumours harbour ecDNA have markedly shorter survival.

Despite being first seen over fifty years, ago, and prescient work on its potential importance, the scale, scope, and impact of ecDNA was not well understood. In fact,
it was thought to be a rare event of unknown significance. The application of powerful new, integrative molecular approaches has shown us, that ecDNAs are present
in nearly half of all human cancer types and at likely in at least a quarter of all cancer patients and they have taught us that ecDNA is indeed, one of the most urgent
problems facing patients with cancer, challenging the success of the targeted therapy approaches, and a problem that is certainly worthy of its nomination as a Cancer
Grant Challenge. Currently, the collective current understanding of how ecDNA form, how they move around the cell, how they evolve to resist treatment, how they
impact the immune system, and how they can be effectively targeted, are lacking. Can we identify actionable co-dependency pathways that are generated by ecDNA
amplification? These are the areas of research focus of research in my laboratory.
We are very collaborative and interactive, with many colleagues around the world. We work very closely with Professor Howard Chang at Stanford, as well as with many other new Stanford colleagues. I have recently joined the faculty of Stanford University as a Professor and Vice Chair for Research for the Department of Pathology, and as an Institute Scholar in ChEM-H, where my lab is based. I am committed to actively contributing not only to the science and its translation for benefit to patients, but also to mentoring trainees at all levels, and helping colleagues, including junior colleagues, develop the skills necessary to navigate the complex landscape of translating science into medicines that will help patients.

Teaching

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)
Kiarash Shamardani, Valentino Sudaryo

Postdoctoral Faculty Sponsor
Jun Tang, Yanbo Wang, Thomas Watkins, Ivy Tsz-Lo Wong

Doctoral Dissertation Advisor (AC)
Rebecca Mancusi

Doctoral Dissertation Co-Advisor (NonAC)
Vishnu Shankar

Publications

PUBLICATIONS

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