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#### **'take 2' On Taok2: Towards the Structure and Mechanism of the Enigmatic Taok2 and Its Interactions with Nuclear Speckle Resident Proteins**

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TAOK2 belongs to the MAP3K family and is the largest of three enigmatic proteins (TAOK1/2/3), combining kinase and protein scaffolding functions to serve a variety of signaling pathways. Recent literature highlighted the involvement of TAOK2 in antiviral immunity, regulation of microtubule dynamics and requirement for nuclear speckle integrity. While TAOKs' roles in physiology and disease are still emerging, progress is hampered by a paucity of structure-function insights. Our studies comprise TAOK2 protein production in different expression systems to understand the potential role of the two-by MS-identified candidate binding partners, which will be studied via biophysical methods. Single-particle cryo-EM and negative stain will provide structural insights into TAOK2's role in nuclear speckles and viral immunity. We recently expanded our efforts to insect-cell expression approaches due to challenges producing recombinant human TAOK2 in bacterial and mammalian systems. We are still optimizing mammalian expression by co-expressing TAOK2 with its two binding partners, hoping to stabilize TAOK2. We envisage that pulldown experiments and co-localization of TAOK2 with its candidate partners via immunocytochemistry will result into deeper insights into the biochemical and biophysical properties of TAOK2 and will be more amenable to structure-function studies than isolated TAOK2.