To overcome therapeutic resistance in \textit{KRAS} mutant lung cancers and \textit{BRAF} mutant colorectal cancers

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\textit{KRAS} is the most commonly identified driver oncogene in lung cancer in the western population, accounting for 20-25\% of all patients. Development of therapeutic strategies to improve the survival of patients with known oncogenic driver alterations is one of the most important needs in the field on oncology. Unlike lung cancers harboring other driver mutations, such as \textit{EGFR}, \textit{ALK} and \textit{ROS1}, there is no effective treatment for \textit{KRAS} mutant lung cancers that are associated with poor prognosis. The therapeutic resistance is attributed in part to molecular heterogeneity of \textit{KRAS} mutant lung cancers, characterized by a variety of distinct \textit{KRAS} point mutations, specific co-mutations, and variable overall mutation burdens associated with poorly defined immune microenvironments.

\textit{BRAF} mutants account for 8-15\% of colorectal cancers in the western population. Although microsatellite instability (MSI) secondary to \textit{BRAF} mutations present in a subset of colorectal cancer patients is associated with favorable patient outcomes, but also reportedly dictates resistance to fluorouracil-based adjuvant therapy. In addition, those with \textit{BRAF} mutated microsatellite stable colorectal cancers are associated with unfavorable outcomes, and \textit{BRAF} inhibitors, which have been proven to effective for \textit{BRAF} mutant melanomas, do not appear to be as much effective for \textit{BRAF} mutant colorectal cancers.

In this talk, I will discuss the current understanding of molecular heterogeneity of \textit{KRAS} mutant lung cancers that is crucial for developing effective targeted therapies, and the updated information on treatment strategies for MSI and non-MSI \textit{BRAF} mutant colorectal cancers.

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