Understanding I-O Resistance

The immune system is extremely complex and can play a powerful role in cancer. Immuno-Oncology (I-O) investigates innovative approaches that aim to harness the body’s natural response to fight cancer with checkpoint inhibitors, a type of immunotherapy drug. While checkpoint inhibitors have changed survival expectations for some patients, not all patients respond to them and some stop responding over time.

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Researchers at Bristol Myers Squibb are pursuing a holistic approach to tackle I-O resistance that encompasses interplay between the immune, tumor and stromal compartments.

- **Foundational mechanisms** under investigation include lack of inflammation, insufficient antigenicity and compensatory immune checkpoints, which research has shown to be drivers of response and resistance.
- **Emerging areas of study** include suppressive immune cell types and suppressive stromal factors, which implicate the role of the tumor microenvironment in resistance.
- Through **tumor intrinsic pathways**, researchers are exploring how to exploit tumor vulnerabilities that lead to I-O resistance (such as through targeted protein degradation) and interrogate oncogenic pathways that mediate immune evasion.

Research in I-O Resistance

The identification of mechanisms of resistance is a key question in immunotherapy resistance that will inform appropriate treatment options for patients. Researchers at Bristol Myers Squibb are actively committed to advancing research into the mechanisms of I-O resistance and are utilizing basket trials, combination therapies and predictive biomarkers to inform potentially personalized strategies with the goal of overcoming I-O resistance.