CANCER DISCOVERY

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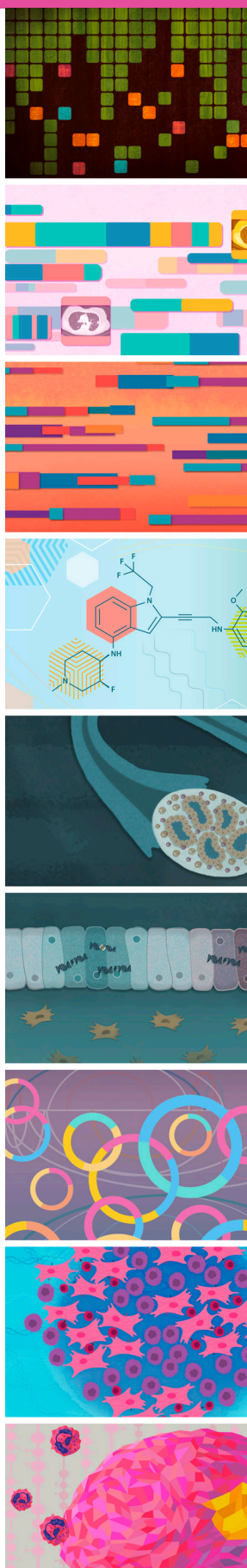

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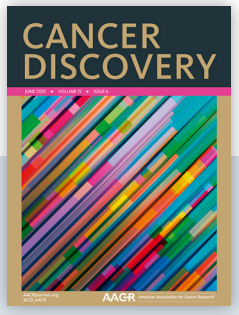

ON THE COVER Seminal studies in mouse skin tumor models, performed over seven decades ago, laid the foundation for the field's conceptualization of tumorigenesis as a two-step process, in which an initiating mutational event poises a tissue for transformation and a subsequent tumor-promoting event, involving proliferation and inflammation, is required for malignant tumorigenesis. While these classical models of tumorigenesis, in which mice receive an initiating dose of a chemical carcinogen, followed by promotional tissue damage, continue to be widely used in research, the molecular mechanisms that underpin the mutational dynamics following the initiating event and the subsequent contribution of tumor-promoting processes to eventual tumor development remain incompletely understood. To shed light on these points, Li and colleagues studied variations of mouse skin tumor models, exposing mice to initiating events, via standard chemical carcinogens or an oncogenic mutation, and providing subsequent tumor-promotional events, in the form of tumor-promoting chemical damage or a range of clinically relevant risk factors such as obesity. These experiments demonstrated that cells carrying thousands of initiating event–induced mutations persist for long periods and only give rise to tumors in the context of a tumor-promoting event. These findings highlight the importance of understanding promotional risk factors in the context of cancer prevention and interception. For more information, see the article by Li and colleagues on page 1115. Artwork by Bianca Dunn.

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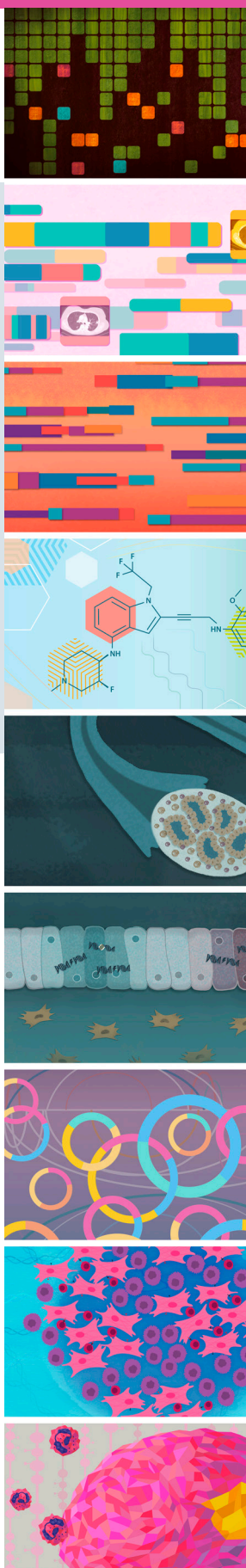

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