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Nota di contenuto	Introduction -- Molecular and cellular functions of CTLA-4 pathway -- Roles of PD-1/PD-L1 pathway: signaling, cancer, and beyond -- Discovery of new immune checkpoints: family grows up -- Mechanisms of resistance to checkpoint blockade therapy -- Molecular events behind adverse effects -- Rational discovery of response biomarkers -- Spatiotemporal changes in checkpoint molecule expression -- Functions of checkpoint molecules beyond immune evasion -- Genetic alterations and checkpoint expression -- Regulations on messenger RNA: wires and nodes -- Folded or degraded in endoplasmic reticulum -- Mono- and poly-ubiquitination: tags for fates -- Lysosome as the black hole for checkpoint molecules -- Phosphorylation: a fast switch for checkpoint signalling -- Palmitoylation as a signal for delivery -- Checkpoints under traffic control: from and to organelles -- Exosome and secretion: action on? -- Macromolecules and antibody-based drugs -- Mechanisms inspired targeting peptides -- Small molecular inhibitors -- Therapeutic development of immune checkpoint blockers

-- Concluding remarks.

Sommario/riassunto

This book systematically reviews the most important findings on cancer immune checkpoints, sharing essential insights into this rapidly evolving yet largely unexplored research topic. The past decade has seen major advances in cancer immune checkpoint therapy, which has demonstrated impressive clinical benefits. The family of checkpoints for mediating cancer immune evasion now includes CTLA-4, PD-1/PD-L1, CD27/CD70, FGL-1/LAG-3, Siglec-15, VISTA (PD-1L)/VSIG3, CD47/SIRPA, APOE/LILRB4, TIGIT, and many others. Despite these strides, most patients do not show lasting remission, and some cancers have been completely resistant to the therapy. The potentially lethal adverse effects of checkpoint blockade represent another major challenge, the mechanisms of which remain poorly understood. Compared to the cancer signaling pathways, such as p53 and Ras, mechanistic studies on immune checkpoint pathways are still in their infancy. To improve the responses to checkpoint blockade therapy and limit the adverse effects, it is essential to understand the molecular regulation of checkpoint molecules in both malignant and healthy cells/tissues. This book begins with an introduction to immune checkpoint therapy and its challenges, and subsequently describes the regulation of checkpoints at different levels. In closing, it discusses recent therapeutic developments based on mechanistic findings, and outlines goals for future translational studies. The book offers a valuable resource for researchers in the cancer immunotherapy field, helping to form a roadmap for checkpoint regulation and develop safer and more effective immunotherapies.