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Cytokine-induced senescence in cancer therapy

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Growing cancers are characterized by infiltrating cancer cells, neo-angiogenesis and a cellular infiltrate with immunosuppressive properties. As it is strongly believed that cancer immune-control strictly relies on the killing of individual cancer cells, and multiple approaches enhance the activity of tumor-reactive killer cells. While generally accepted, this view conflicts with the observation that efficient anti-cancer immunity rarely eradicates cancer. Thus, efficient immunotherapy of metastatic melanoma causes cancer regression and stable growth arrest rather than cancer eradication. Recent data now show that adaptive immunity can arrest cancers through signals mediated by the T_H1 cytokines interferon (IFN) and tumor necrosis factor. When signaling together, IFN and TNF can induce a permanent growth arrestin cancers that is named senescence. Simultaneous action of IFN and TNF activates the p16/Rb-senescence pathway in a large spectrum of cancers. Efficient activation ofthe p16/Rb-senescence pathway drives even advanced cancers into senescence. Importantly, the T_H1 cytokines IFN and TNF also induce senescence in a large spectrum of human cancers. Such senescent cancers share many similarities with premalignant tumors, including their failure to grow in an immune-incompetent environment. As cytokine-induced senescence can also arrest established cancers, treatment of established cancers by T_H1 cytokines is currently investigated.

Biography

Martin Rocken is Professor and Chairman of a large dermatology department, with a strong focus on clinical, experimental and translational oncology. He is member of major societies namely the *German Academy of Sciences*. He is/was executive board member of major journals, funding and research organizations. His lab, supported by public funds, characterized major signals allowing the antigen-specific induction of either TH1 or TH2 cells *in vivo*, first in mice and then in humans, and established immune-based therapies. Recently, they first described that immunity can arrest cancer by inducing senescence, a permanent growth arrest, even in the absence of killing.

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