Selective targeting of angiogenesis and of tumor stroma

Project ID: 503233
Funded under: FP6-LIFESCIHEALTH

Project details

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<td>LIFESCIHEALTH-2.2 - Combating cancer</td>
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Objective

The majority of pharmacological approaches for the treatment of solid tumours suffers from poor selectivity, thus limiting dose escalation (the doses of drug required to kill tumour cells cause unacceptable toxicities to normal tissues). The situation is made more dramatic by the fact that the majority of anticancer drugs accumulate preferentially in normal tissues rather than in neoplastic sites, due to the irregular vasculature and to the high interstitial pressure of solid tumours.

One avenue towards the development of more efficacious and better tolerated anti-cancer drugs relies on the targeted delivery of therapeutic agents to the tumour environment, sparing normal tissues.

This proposal focuses on the:
- identification and validation of molecular targets which are selectively expressed in the stroma and in neo-vascular sites of aggressive solid tumours. Endothelial cells and stromal cells are genetically more stable than tumour cells and can produce markers, which are ideally suited for tumour targeting strategies
- isolation of high-affinity binding molecules [small organic compounds, human antibodies], specific for markers of angiogenesis and/or the stroma, and are capable of selective localization in the tumour environment, after intravenous administration.
- development of therapeutic strategies, based on specific binding molecules capable of selective localization around tumour vascular structures and/or in the tumour stroma.

This experimental strategy requires a range of diverse experimental techniques, for the identification of markers, for the isolation of binding molecules, and for their conversion into imaging and therapeutic products. Our approach has the potential advantage that immunohistochemistry, imaging and biodistribution data provide information about the selectivity of the anti-cancer drugs at several stages of the drug development process, and allow a rational optimisation of the most promising lead compound.

Related information

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Last updated on 2012-10-19
Retrieved on 2019-06-30

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