IN BRIEF

COMPUTATIONAL BIOLOGY

Computational design of antibody-affinity improvement beyond *in vivo* maturation.

Lippow, S. M. *et al. Nature Biotechnol.* **25**, 1171–1176 (2007)

High-affinity antibody binding is important for increasing drug efficacy. Lippow and colleagues present an iterative computational design procedure that focuses on electrostatic binding contributions and single mutants. A tenfold affinity improvement was engineered into the anti-epidermal growth factor receptor drug cetuximab, and a 140-fold improvement in affinity was obtained for an antilysozyme antibody. The generality of the methods was demonstrated through identification of known affinity-enhancing mutations in bevacizumab and an anti-fluorescein antibody.

CANCER

Distinct populations of cancer stem cells determine tumor growth and metastatic activity in human pancreatic cancer.

Hermann, P. C. *et al. Cell Stem Cell* **1**, 313–323 (2007)

The role of stem cells in pancreatic cancer metastasis is uncertain. Hermann and colleagues found that human pancreatic cancer tissue contains cancer stem cells defined by CD133 expression that are exclusively tumorigenic and highly resistant to standard chemotherapy. A subpopulation of migrating CD133⁺ CXCR4⁺ cancer stem cells was identified that was essential for tumour metastasis. Depletion of the cancer stem-cell pool for migrating cells virtually abrogated the metastatic phenotype of pancreatic tumours without affecting their tumorigenic potential. So, strategies aimed at CXCR4 or its ligand may have applications to inhibit metastasis of cancer stem cells.

DRUG ABSORPTION

Is PAMPA a useful tool for discovery?

Galinis-Luciani, D. *et al. J. Pharm Sci.* **96**, 2886–2892 (2007)

PAMPA-critical factors for better predictions of absorption.

Avdeef, A. *et al. J. Pharm Sci.* **96**, 2893–2909 (2007)

To predict intestinal absorption of drugs, several experimental models can be used, such as Caco-2 (an intestinal cell model), parallel artificial membrane permeation assay (PAMPA) and octanol–water coefficients (for example, logP and logD values).

Two recent papers investigate the utility of such assays in the drug discovery process. Galinis-Luciani and colleagues examined published PAMPA data and calculated logD values, together with experimental PAMPA data for 40 small molecular mass drugs. It was found that although PAMPA yields information about drug lipophilicity, this could be derived in a simpler manner from calculated logD values. Moreover, PAMPA loses advantages such as speed over Caco-2, which also provides information about active transport. The authors conclude that PAMPA may be a limited asset. In the second paper Avdeef and colleagues present an alternative view. PAMPA had better predictivity for oral absorption, and PAMPA measurement was more rapid and cost effective than Caco-2 and logP. PAMPA conditions were critical to generate high quality and relevant data — including permeation time — and careful data interpretation was necessary. The authors conclude that PAMPA gives improved intestinal absorption predictions.

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