GERMAN CANCER RESEARCH CENTER IN THE HELMHOLTZ ASSOCIATION

Research for a Life without Cancer

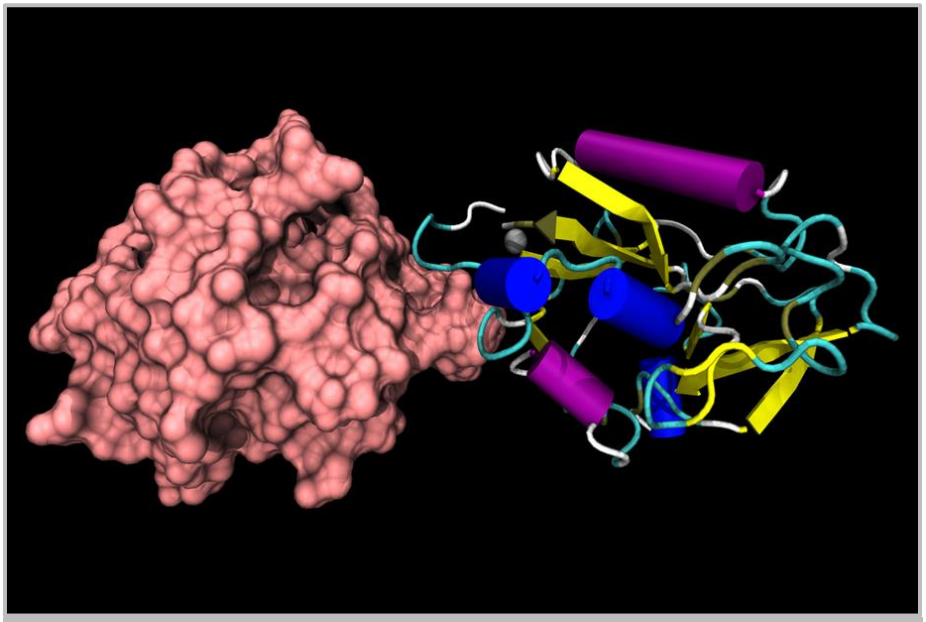
TECHNOLOGY OFFERS

Oligomerization Improves Endostatin as Antiangiogenic and Anticancer Drug (P-1000)

Synthetic dimerization of endostatin via fc-conjugation to improve pharmacokinetics and efficacy

EXECUTIVE SUMMARY

We identified a novel molecule, NC1 rather than monomeric endostatin to be the key physiologic molecule exerting antiangiogenic effects. We further provide rational that synthetic dimerization of endostatin via Fc-conjugation not only improve its pharmacokinetics and therefore the biologic efficacy but also better mimics the effects of the natural trimeric NC1 as compared to monomeric "conventional" endostatin. We demonstrated that oligomerization of endostatin as observed in NC1 is important for its binding to a large number of extracellular matrix proteins including Fibronectin and cytokines such as VEGF, which are important ligands for exertion of an antiangiogenic property.



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https://commons.wikimedia.org/wiki/File:Endostatin_1BNL.png

Category	Indication	Development stage	Seeking
Therapeutics	Cancer	Trial	Licensing

BENEFITS

- Endostatin is well known and therefore approved in clinical trials
- Established endostatin has as monomer poor efficacy
- Oligomerization of endostatin improves pharmacokinetics

TECHNOLOGY BACKGROUND

Endostatin is an antiangiogenic protein first discovered in Folkman's laboratory at Childrens Hospital, Harvard Medical School, and Boston. The antitumor properties of this protein are well established. However, the amount of protein required for injection in patients was beyond production feasibility due to the poor pharmacokinetics of endostatin monomer. We have shown that the problem of poor pharmacokinetics can be solved by using the Fc-domain of IgG being conjugated to endostatin, a component of all monoclonal antibodies approved for patients with a number of diseases including cancer. As a result of employing Fc-endostatin, the half-life in mice was increased to 2 weeks instead of 2 hours for endostatin alone, consistent with pharmacokinetics of monoclonal antibodies.

DEVELOPMENT STAGE

A clinical trial based on Fc-NC1 or Fc-endostatin will be carried out in order to enable us to evaluate the efficacy of antiangiogenic endostatin.

APPLICATIONS

Established endostatin resulted in poor efficacy in clinical trials. In contrast, oligomerization of endostatin toward the natural fragment of collagen 18 (NC1) can improve both, pharmacokinetic as well as the spectrum of argeting molecules for a broader use of endostatin as antiangiogenic and anticancer drug.

INTELLECTUAL PROPERTY

Patent application submitted.

- PCT application published as WO2013026913A2
- European equivalent EP2747775A2 is pending, US20140302026A1 is pending, granted as CN104271151B in China, JP2014529605A is pending.

PUBLICATIONS & REFERENCES

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