

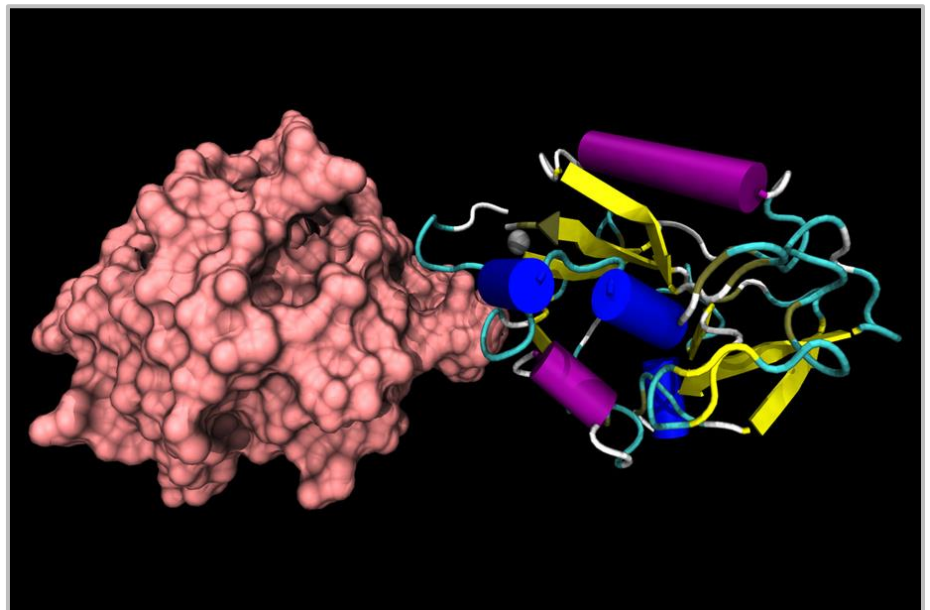
## TECHNOLOGY OFFERS

# 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 rationale 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.



Ayacop, Wikimedia, CC0  
[https://commons.wikimedia.org/wiki/File:Endostatin\\_1BNL.png](https://commons.wikimedia.org/wiki/File:Endostatin_1BNL.png)

### Category

Therapeutics

### Indication

Cancer

### Development stage

Trial

### Seeking

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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### DKFZ Contact:

Dr. Frieder Kern  
Deutsches Krebsforschungszentrum  
Innovation Management T010  
Email: F.Kern@dkfz.de  
Tel.: +49-(0)6221-42-2952  
Fax: +49-(0)6221-42-2956

## ABOUT THE DKFZ INNOVATION MANAGEMENT

Working at the interface of research and industry, the Innovation Management of the German Cancer Research Center (DKFZ) helps to get new cancer medications, diagnostic tests, and research instruments onto the market as quickly as possible.

The DKFZ with its more than 3,000 employees is the largest biomedical research institution in Germany. At the Center more than 1,300 scientists investigate how cancer develops, identify cancer risk factors and endeavor to find new strategies to prevent people from getting cancer. They develop novel approaches to make tumor diagnosis more precise and treatment of cancer patients more successful. DKFZ is a member of the Helmholtz Association of National Research Centers, with ninety percent of its funding coming from the German Federal Ministry of Education and Research and the remaining ten percent from the State of Baden-Württemberg