TIMP-2 Angio-Inibitory and Tumor Chemo-sensitizing Activities

TEDCO/NIH/NCI Technology Showcase

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Technology

- Tissue Inhibitor of Metalloproteinases-2 (TIMP-2) inhibits angiogenesis independently of metalloproteinase inhibitory activity (Angio-Inibitory activity).
- Angio-Inibitory activity is mediated by binding to cell surface receptor.
- Cell surface receptor is identified as alpha3 beta1 ($\alpha 3\beta 1$) integrin.
- TIMP-2 peptides binding to $\alpha 3\beta 1$ have been identified.
- These peptides retain angio-inhibitory activity *in vivo* at low micromolar concentrations.

Technology

- TIMP-2 inhibits growth of tumor xenografts independent of metalloproteinase inhibitory activity (Ala+TIMP-2).
- The mechanisms of this effect involves tumor differentiation and enhanced tumor cell apoptosis.
- TIMP-2 induces expression of genes marking tumor differentiation (E-cadherin).
- TIMP-2 inhibits expression of genes associated with tumor invasion & metastasis(e.g. twist, Notch-4, Id-1 and Id-3 genes).
- TIMP-2 enhances tumor cell apoptosis *in vitro* and *in vivo.*
- TIMP-2 enhances cytotoxic drug-induced tumor cell apoptosis (chemo-sensitizing).

Technology Applications

- **TIMP-2 Angio-Inibitory peptides would be synthesized and tested for anti-tumor activity *in vivo.***
- **TIMP-2 Angio-Inibitory peptides would be utilized as a starting point for development of retro-inverso peptides with similar biological activity.**
- **TIMP-2 Angio-Inibitory peptide sequences/structure would be utilized to begin identification of small molecule analogs *in silico.***
- **TIMP-2 Angio-Inibitory peptides would be utilized in high throughput screening of small molecule libraries to identify compounds with either Angio-Inibitory or Pro-angiogenic activities.**

Technology Applications

- **TIMP-2 and Ala+TIMP-2 would be used as adjuvants to potentiate the activity of cytotoxic drugs and reduce side effects.**
- **TIMP-2 peptides with similar biological activity would be identified.**
- **TIMP-2 peptides with direct tumor differentiating activity would be utilized as adjuvant therapy in conjunction with conventional cytotoxic chemotherapies.**
- **TIMP-2 peptides with these biological activities would serve as a starting point for development or retro-inverso peptides with similar biological activity, *in silico* development of small molecule analogs, as well as development of high throughput screening assays for small molecule analogs.**

Commercial Applications

- **Commercial applications include TIMP-2 Angio-Inibitory peptides/analogs for treatment of chronic diseases with a significant angiogenic component such as:**
  - Carcinoma
  - Diabetic retinopathy
  - Psoriasis
  - Rheumatoid Arthritis, etc.
- **Commercial applications include adjuvant to conventional cytotoxic chemotherapy using Ala+TIMP-2 protein or TIMP-2 peptides:**
  - That have direct cytotoxic activity against tumor cells
  - Enhance tumor cell apoptosis
  - Potentiate cytotoxic chemotherapy and reduce side effects (Chemo-sensitizing effect)

Collaboration Opportunities

- **Both Licensing and/or CRADA opportunities are available for "Angio-Inibitory Peptides Derived From Human TIMP-2".**

  Reference: Employee Invention Report E-186-2005/Patent Application Filed

- **Both Licensing and/or CRADA opportunities are available for "Differentiation-induction and Chemo-sensitizing Therapy of Cancer Using Tissue Inhibitor of Matrix Metalloproteinases-2 (TIMP-2) Mutants and Peptides".**

  Reference: Employee Invention Report E-297-2007/Patent Application Filed

Contact Information

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