Metレセプター過剰発現に基づく悪性中皮腫の治療とNK4による制癌の至適化

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Research Abstract	私達はHGFアンタゴニストとしてNK4を見いだすとともに、NK4は血管新生阻害作用も有する2機能性分子として、複数の癌に対して浸潤・転移阻害、成長阻害、延命といった制癌作用を発揮することを明らかにした。本研究は悪性中皮腫に対するNK4の制癌作用を明らかにすることを目的とし、平成19年度において以下の成果を得た。 1.ヒト悪性中皮種細胞(7種類)すべてにMet受容体の発現が認められ、NK4はHGFに依存したMet受容体のチロシンリン酸化、中皮種細胞の遊走、コラーゲンゲル内浸潤を阻害した。 2.NK4はコラーゲンゲル内で培養した悪性中皮種細胞の増殖、ならびに軟寒天培地でのコロニー形成を抑制した。 3.ヒト悪性中皮種の皮下移植モデルを用いて、NK4発現用アデノウイルスベクターを腫瘍内に投与した。NK4遺伝子治療により腫瘍血管密度が低下し、腫瘍の成長は対照の26%に阻害された。NK4による成長抑制には、腫瘍血管新生阻害に加え、悪性中皮腫細胞の増殖に対する直接的な抑制作用が関与していると考えられる。 4.NK4は血管内皮細胞に対してフィブロネクチンの細胞表面構築を阻害した。そこでNK4に親和性のある血管内皮細胞由来の細胞膜分子の精製・同定、共局在の解析、発現抑制などによりNK4結合分子を絞り込んだ。NK4はMet/HGF受容体とは異なる分子に結合することによってフィブロネクチンの細胞外構築を阻害する結果、増殖・生存を支えるインテグリンを介したシグナルを阻害することによって血管新生を阻害すると考えられる。 NK4による悪性中皮腫細胞の増殖・コロニー形成阻害はNK4の新たな生物活性であり、どのようなメカニズムで抑制作用を示すか解析を進めることが重要である。一方、NK4は胸膜・腹膜における悪性中皮腫の成長ならびに浸潤・伸展を抑制する制癌法になることが期待される。

Report (2 results)

2007 Annual Research Report

2006 Annual Research Report

Research Products (49 results)

All | 2008 | 2007 | 2006

All | Journal Article | Presentation | Book | Patent(Industrial Property Rights)

[Journal Article] Generation of engineered recombinant hepatocyte growth factor cleaved and activated by Generase I. 2008

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[Journal Article] A genomic analysis of adult T-cell leukemia. 2007

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[Journal Article] NK4, an antagonist of hepatocyte growth factor (HGF), inhibits growth of multiple myeloma cells: Molecular targeting of angiogenic growth factor. 2007

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[Patent(Industrial Property Rights)] 喘息治療剤 **2007**

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