はまだ不明であるが、これまでVEGFには血管新生能以外に神経細胞保護効果があることが報告され、ALSモデル動物である変異SOD1 Tgマウスに投与することで、その発症を遅延させ、寿命を延長することが示されている(Storkebaum *et al*, Nat Neurosci 05)。血管内非細胞においては、VEGFが血管新生能を発揮するにあたってANGが必要であるという報告もあり(Kishimoto *et al*, Oncogene 05)、VEGFとANGが共通の経路を有している可能性もある。今後、ANG-siRNA Tgマウスを用いて、ALSの病態とこれら血管新生因子との関連を明らかにして、新たなsiRNAの標的分子を見つけていきたい。

E. 結　論

1) siRNA治療において抑制された内因性の野生型遺伝子の発現を、siRNA抵抗性野生型遺伝子を用いて補った結果、変異遺伝子に選択的な遺伝子抑制に*in vivo*で成功した。
2) AAVベクターでshRNAを過剰に発現させると著明な肝障害が誘導されるが、shRNAの発現量を適切に調節することで副作用を回避し標的となる内因性遺伝子の発現を抑制することに成功した。
3) 新しいALSのモデル動物マウスとして、複数存在するANGを同時に効率よく抑制するsiRNAを設計し、ANG-siRNA Tgマウスのキメラマウスを作製することに成功した。

F. 健康危険情報

なし

G. 研究発表

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H. 知的所有権の取得状況(予定を含む)

1. 特許出願

横田隆徳，水澤英洋，他．あらゆる遺伝子を標的とすることを可能としたsiRNAトランスジェニックマウス(ノックダウンマウス)の新規作製方法(特許出願番号2007-118962)

2. 実用新案登録

なし

3. その他

なし

Ⅳ. 研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表

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