A Novel Anti-angiogenesis Therapy Using Integrin Targeted Nanoparticles

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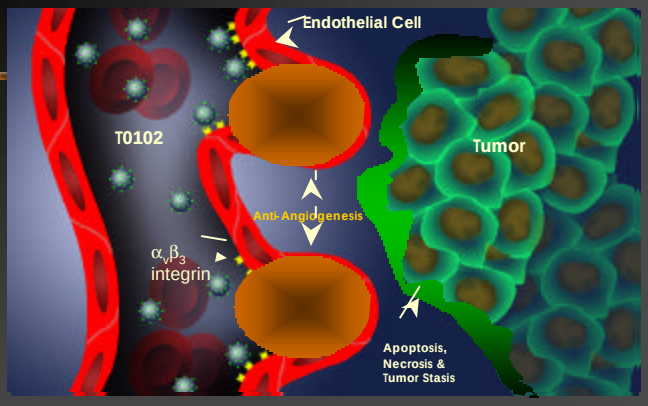
Anti-angiogenesis approach using T0102

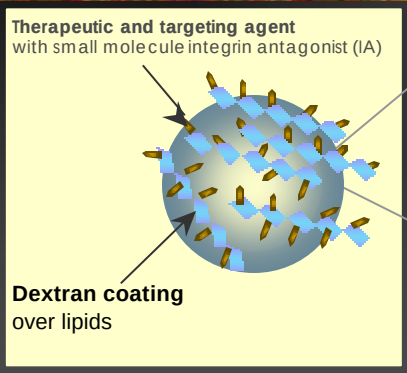


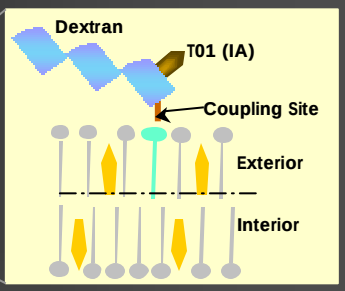
Advantages of the nanoparticle approach:

- increased half-life
- vascular confinement
- enhanced efficacy

T0102 Composition

T01: IA & T0002: Dextran-Coated Liposomes (DCL)





= 5 % DPPE-Succinate

= 55% DPPC

= 40% Cholesterol

- particle size of ~100 nm

Study Design

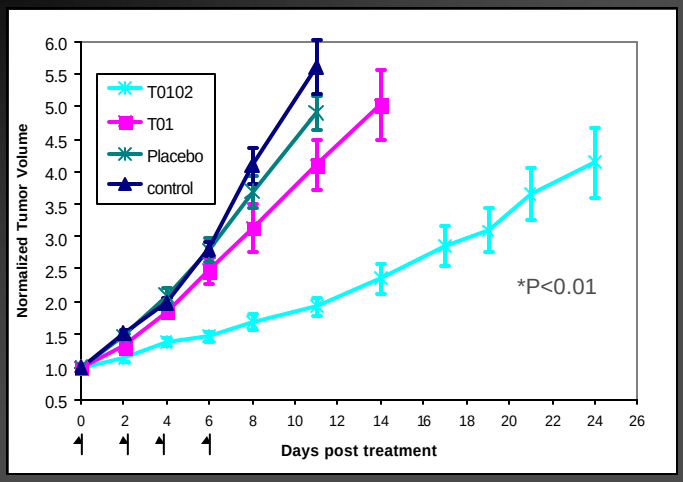
- Tumor model: human M21 melanoma xenograft
- Treatment regimen:
  - T0102 (15 mg/kg, iv)
  - cyclo RGDfV (15 mg/kg, ip)
  - T01 (15 mg/kg, iv)
  - Buffer and placebo control

  Four doses administered every other day for a week
- Tumor growth delay

  TUNEL assay and anti-CD31 staining

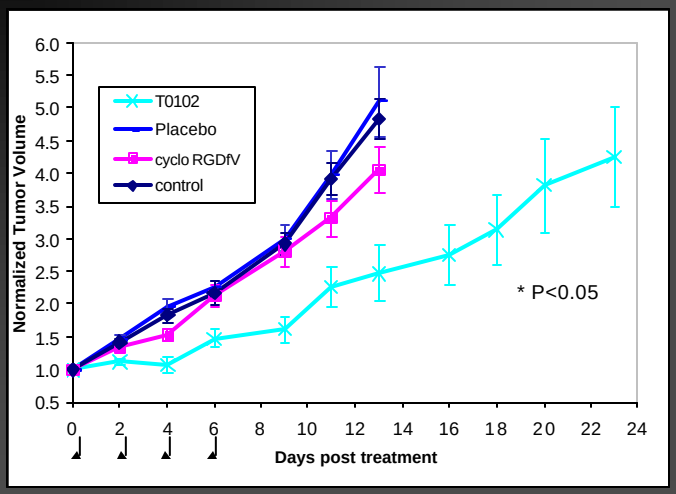
  Toxicity

Superior efficacy of T0102 compared to free T01 (IA)



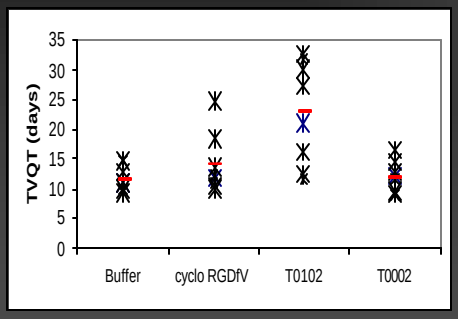
- n=9, error bars indicate ± standard error

Superior efficacy of T0102 compared to cyclo RGDfV



- n=8, error bars indicate ± standard error

T0102 Increases Tumor volume Quadrupling Time (TVQT)

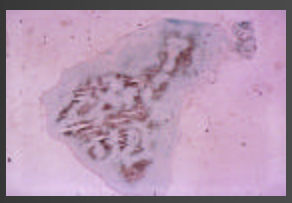


Summary of P-values obtained using Tukey's Pairwise Comparisons

	Buffer	cyclo RGDfV	Placebo
cyclo RGDfV	>0.05		
Placebo	>0.05	>0.05	
T0102	0.002	0.026	0.002

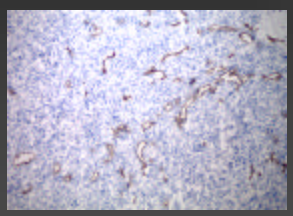
T0102 Induces Tumor Apoptosis and Reduces Tumor Vessel Density

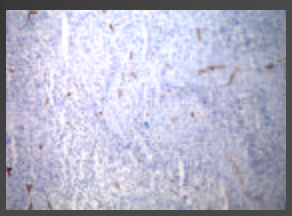
TUNEL (15X)



(20X)

Anti-CD31 (100X)





(100X)

Buffer control T0102

- **40% reduction in vessel count with T0102 vs. control (179 vs. 299)**

Summary

- T0102 significantly inhibited tumor growth, and showed superior efficacy compared to free T01 in M21 model.
- T0102 treatment caused extensive tumor apoptosis and reduced tumor vessel density ~40% in M21 model, which revealed the anti-angiogenic mechanism of this therapeutic approach.
- Necropsy data indicated that there were no gross or histopathological changes in animals following T0102 therapy.
- These encouraging results demonstrate the advantage and potential therapeutic application of active drug targeting therapy using the nanoparticle approach.

Acknowledgements

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  - Michael Zhang
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