Blowing-up Lung Cancer
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- Pulmonary route of administration
  - Inhalable Nanoparticles
  - Active release from the carrier
  - Nanotoxicology of Drug Delivery Systems
  - In vitro results
  - In vivo results
  - Summary/Conclusions

Lungs as Treatment organ
- Asthma (Hardy and Chadwick, 2000)
- Cystic fibrosis (Garcia-Contreras and Hickey, 2002)
- Lung cancer (Rao et al., 2003)
- Tuberculosis (Pandey and Khuller, 2005; Zahoor et al., 2005)

DEPOSITION MECHANISM

- General air flow through the respiratory tract
- Large particles will impact in the upper respiratory tract (>5 um)
- Small particles will have no deposition because of Brownian diffusion (<1 um)
- Sedimentation in the alveolar region (1-5 um)

Pulmonary Nanoparticle delivery
- Solid colloidal particles < 1000 nm
- But how can you deliver them to the lungs?
- Suitable size is between 1000 and 5000 nm?

We had to go back to the lab and do some experiments

THE CONCEPT

Suspension of lactose and nanoparticles
Spray drying

Respirable lactose aerosol particles containing nanoparticles

Biological activity of the Nanoparticles

"Blowing Up Lung Cancer
Nanoparticle cluster bomb" delivers cancer drugs right to target

Passive dissolving Carrier Matrix

- Polycyanoacrylate nanoparticles mostly clustered in different spots within the lactose carriers. The mean sizes of both nanoparticle types were characterized at two different times: before they were spray-dried and after they were redissolved from the spray-dried powders. A tendency of the particles to agglomerate was observed.

NEW SYSTEM OF CARRIER PARTICLES

- Effervescent carrier particles:
  
  Lactose
  Sodium Carbonate
  Acid Citric
  Ammonia
  Water

FORMATION

Study design

- Female 4-5 weeks old BALB/c nude mice
- NCI-H460 injection
- Small lung metastatic nodules develop in 15 days
- Treatment over 4 weeks with
  - Free Drug
  - Inhalable NPs
  - Blank NPs
  - No treatment

Expectation

- The cancer will spread throughout the body
- The animals will die because of cancer in other organs
- The Lungs might show less cancer compared to other tissues due to the treatment

Conclusions

- New dry powder technology is available to deliver NP or drugs to the lungs
- Improved pulmonary drug delivery for cytotoxic molecules is possible using nanoparticles
- Drug delivery is the key to improve (lung cancer) treatments.

Articles

- Nanoparticles: characteristics, Mechanisms of Action and Toxicity in Pulmonary Drug Delivery - A Review
  S. Gill, R. Löbenberg, T. Ku, S. Azarmi, W. Roa and E.J. Penner
  J Biomed Nanotechnology 2007
- Effervescent Dry Powder Aerosols for Respiratory Drug Delivery
  Leticia Ely, Warren H. Finlay, Wilson H. Roa, Raimar Löbenberg
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- Biophysical investigation of nanoparticle interactions with lung surfactant model systems
  Tabitha Ku, Shirzad Azarmi, Diana Stuart, Raimar Löbenberg, Leticia Ely, Warren Roa and Elmar J. Penner
  J Biomed Nanotechnology Volume 2, Numbers 3-4, October/December 2006, pp. 245-252
- Formulation and Characterization of Drug-loaded Nanoparticles Carried by Dry Powder Aerosol Particles
  Shirzad Azarmi, Xia Tao, Hua Chen, Zhao Lin Wang, Warren H. Finlay, Raimar Löbenberg, Wilson H. Roa
- Formulation and characterization of inhalable nanoparticles and cell uptake studies in 1080 lung carcinoma cells
  Arun K. Pratap, T. Ku, Shirzad Azarmi, Raimar Löbenberg
- Formulation and Characterization of Spray-Dried Powders Containing Nanoparticles for Aerosol Delivery to the Lung
  Jeffrey O. Hanson, Yu Zhang, Warren H. Finlay, Wilson H. Roa, and Raimar Löbenberg
- Dry Powder Inhalation Aerosols Containing Nanoparticulate Doxorubicin
- Formulation and Characterization of Spray-Dried Powders Containing Nanoparticles for Aerosol Delivery to the Lung
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Any Questions

Dreams come true. Without that possibility, nature wouldn’t incite us to have them.

John Updike