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## **P-206 Potential Non-invasive Tracheobronchial Targeted Delivery of DNA by PLGA Microspheres**

*Farahidah Mohamed, Chris van der Walle*  
*Department of Pharmaceutical technology, Kulliyah of Pharmacy*  
*International Islamic University Malaysia*

DNA-based intervention is potentially effective at treating chronic respiratory diseases. However, DNA is a delicate material requiring suitable carrier system for optimal inclusion into the body's system. Inhalable PLGA microspheres is discussed here as a more efficient mode of DNA delivery via pulmonary. Large scales of DNA-loaded PLGA microspheres were fabricated by two-step w/o/w double-emulsion solvent evaporation using two types of surfactants (Tween 20 & Pluronic L92). Microspheres were harvested by centrifugation, washed 3 times with distilled water, snap frozen in liquid nitrogen and lyophilised overnight. Lyophilised microspheres were kept at 4 °C in a sealed container with silica gel. Four independent batches for each surfactant type were fabricated. Surface morphologies of lyophilized microspheres were observed by scanning electron microscope (JEOLJSM-6400, Japan). Microsphere diameter (size) and distribution were measured prior to freeze-drying by laser diffractometry (Mastersizer 2000, Malvern Instruments, UK). The bulk density of lyophilised microspheres was calculated from the volume occupied by a known mass of microspheres loaded into a measuring cylinder and tapped 5000× (Tap Density Volumeter, Copley Scientific, UK). Volume measurements were repeated for four independent batches of microspheres, subsequently used in the inhaler experiments. Deposition pattern was evaluated using a Multi-Stage Liquid Impinger (MSLI) (Copley Scientific), interfaced with Monodose™ inhaler containing a hard gelatin capsule, pre-loaded with 30 mg ± 2 of dry microspheres. DNA concentration was measured by UV absorbance. The fabrication was optimised so that the median diameter, produced, fell within the desired range for inhalational of the particles, i.e. geometric diameter of > 5 µm (below which, particle tend to be exhaled automatically) but < 10 µm (to avoid RES uptake). Although the size produced by both surfactants were significantly different, but both retained similar aerodynamic diameters due to insignificant different in their density. Substantial deposition of microspheres at tracheobronchial region is a strong evidence to suggest these PLGA microspheres as a better generic carrier to deliver active DNA-based therapy to the region.

## **P-215 Low Level of BRCA-1 Mutations in Malaysian Breast Cancer Patients**

*Salih F, Ghazi A, Mustafa MIA, Amjad N, Cheung S. H.*  
*Basic Medical Science, Kulliyah of Medicine*  
*International Islamic University Malaysia*

Women who carry BRCA1 mutations have a probability of about 80% for developing breast cancer, and 40 to 60% for developing ovarian cancer during their lifetime. We screened for mutations in exon 11A of the BRCA1 gene in 35 breast cancer patients with family history of breast cancer and 35 without family history. The control groups included 35 normal women with family history of breast cancer and another 35 with no family history. Genomic DNA was extracted and segment A of exon 11 was amplified by polymerase chain reaction (PCR) using published primers.

Protein Truncation Test (PTT). was utilized to screen for mutations in the amplicons. Sequencing was also carried out for selected samples to confirm the results. PTT mutations were detected in neither patients nor control groups.