THERAPY AND DIAGNOSIS OF BLADDER DISEASES

Bladder cancer is characterized by an exceptionally high rate of recurrence up to 80% in spite of surgical resection of the tumor. Patients require lifelong surveillance rendering bladder cancer the most expensive cancer therapy. To overcome the rather short residence time of drugs in the bladder cavity, non-specific bioadhesion as well as a specific one exploiting the aberrant gylcosylation pattern upon malignant transformation might represent promising strategies towards improved therapy.

Urinary tract infections belong to the most common infectious diseases worldwide and 50% of the female population experience at least one infection in their lifetime. 95% of these infections are caused by uropathogenic Escherichia coli adhering to high-mannose oligosaccharides of the urothelial membrane via their FimH-pili. Thus, a biomimetic approach using specifically carbohydrate binding proteins to mediate bioadhesion of drug delivery systems on the urothelium is the rationale for development of more efficacious formulations.

Tools:

- Cultivation of cell lines: Human healthy bladder cells (SV-HUC) and malignant ones such as 5637 (grade 2), HT-1376 and T24 (grade 3) as single cells and monolayers on glass and plastic labware
  Establishment of glycosylation pattern even under flow conditions, binding and internalization of wheat germ agglutinin
  Analytical techniques: flow cytometry, fluorescence – and deconvolution microscopy, fluorescence based techniques
- Porcine primary bladder cells: Establishment of protocols for isolation and cultivation of single cells and monolayers cultivated on transwells
- Porcine bladder specimens: glycosylation pattern as a basis for development of drug delivery systems
- Uropathogenic E.coli: mannose-sensitive GFP-expressing and non labeled E.coli
- Drug delivery systems:
  - *Polymeric prodrugs* consisting of a polymer backbone, WGA as a targeter and cytostatics or antibiotics – cytoadhesion and internalization confirmed
  - *Microparticles*: 3µm and 10µm PLGA particles loaded with bacteriostatic agents surface-decorated with lectins – improved adhesion on monolayers of healthy and malignant cells; burst release within the first two days followed by nearly constant release for two weeks.

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