Gene Therapy: Science, History, and Implications for Pharmacy

Theresa A. Mays, B.S., PharmD., BCOP

Learning Objectives

- Define the goals & principles of gene therapy
- Explain history of gene therapy clinical trials, disease, & conditions that have been studied, & areas of future research
- Describe factors that pharmacy should address

Background of Gene Therapy

- Gene therapy involves the introduction of genetic material into a patient with a therapeutic intent

Roth RI & Fleischer NM. JAPhA. 2002;42:692-8

Background of Gene Therapy

- First trial conducted in 1990
- Majority of open clinical trials are in oncology

Roth RI & Fleischer NM. JAPhA. 2002;42:692-8

Background of Gene Therapy

- Potential therapy option for:
  - Single genetic conditions, such as severe combined immunodeficiency diseases
  - Multifactorial genetic conditions
  - Acquired genetic conditions

Roth RI & Fleischer NM. JAPhA. 2002;42:692-8

Background of Gene Therapy

- Biosafety levels
  - Guidelines to protect both personnel & environment

http://www.cdc.gov/OD/ohs/pdffiles/bsl123.pdf

Background of Gene Therapy

- Level 1 – nonpathogenic
  - Examples: *Bacillus subtilis, E. coli*
  - Basic requirements

http://www.cdc.gov/OD/ohs/pdffiles/bsl123.pdf

Background of Gene Therapy

- Level 2 – pathogenic if injected, inhaled, or ingested or exposed to mucous membranes
  - Examples: measles virus, hepatitis B virus

http://www.cdc.gov/OD/ohs/pdffiles/bsl123.pdf

Background of Gene Therapy

- Level 3 – pathogenic, with potential for serious or lethal disease & potential for aerosol transmission
  - Examples: *M. tuberculosis, Coxiella burnetii*

http://www.cdc.gov/OD/ohs/pdffiles/bsl123.pdf

Background of Gene Therapy

- Level 4 – dangerous or of unknown but potentially life-threatening disease potential & potential for aerosol transmission
  - Example: *Ebola*

http://www.cdc.gov/OD/ohs/pdffiles/bsl123.pdf

Background of Gene Therapy

- Vectors can be grouped broadly as:
  - Viral
  - Liposomal
  - Artificial Chromosomal
  - Other nucleic acid

Roth RI & Fleischer NM. JAPhA. 2002;42:692-8

Background of Gene Therapy

- Retrovirus Vectors
  - Advantages
  - Disadvantages
  - Biosafety

http://files.myweb.med.ucalgary.ca/files/91/files/unprotected/Bio-Safety_of_Viral_Vectors_for_Gene_Therapy.pdf

Background of Gene Therapy

- Adenovirus
  - Advantages
  - Disadvantages
  - Biosafety

http://files.myweb.med.ucalgary.ca/files/91/files/unprotected/Bio-Safety_of_Viral_Vectors_for_Gene_Therapy.pdf

Background of Gene Therapy

- Adeno-Associated Virus
  - Advantages
  - Disadvantages
  - Biosafety

http://files.myweb.med.ucalgary.ca/files/91/files/unprotected/Bio-Safety_of_Viral_Vectors_for_Gene_Therapy.pdf

Issues with Gene Therapy

- Technical limitations
  - Identification of gene
  - Manufacturing delivery system
  - Introducing gene into recipient
  - Appropriate gene expression in subject

Roth RI & Fleischer NM. JAPhA. 2002;42:692-8

Issues with Gene Therapy

- Patient safety
  - Acute toxic responses
  - Fatalities
  - Potential interactions between introduced gene and the recipient's genes
  - Latent effects of therapy

Roth RI & Fleischer NM. JAPhA. 2002;42:692-8

Issues with Gene Therapy

- Ethical
  - How to select recipients
  - Essential genetic repair versus non- essential genetic improvement
  - Consequences of intended or inadvertent germ-line modifications

Roth RI & Fleischer NM. JAPhA. 2002;42:692-8

Issues with Gene Therapy

- Regulatory
  - Longer follow up of patients necessary
  - Who pays?

Roth RI & Fleischer NM. JAPhA. 2002;42:692-8

Issues with Gene Therapy

- Pharmacy
  - Traditional role
  - Treatment coordinator / communicator

Roth RI & Fleischer NM. JAPhA. 2002;42:692-8

Pharmacy and Gene Therapy

- Risk assessment
- Majority of gene products under investigation will be classified as a biosafety level 2

DeCederfelt, et al. *AJHP* 1997;54:1604-10

Pharmacy and Gene Therapy

- Compounding worksheet
- Calculations performed prior to mixing
- Compounding area designated as biohazardous

DeCederfelt, et al. *AJHP* 1997;54:1604-10

Pharmacy and Gene Therapy

- Equipment needed
  - BSC class II, type B
  - -80°C freezer
  - 10% bleach solution
  - Autoclave
  - Ice / ice buckets
  - Sterile admixture supplies
  - Surgical gowns
  - Masks
  - Hair covers
  - Vortex-type mixer

DeCederfelt, et al. *AJHP* 1997;54:1604-10

Pharmacy and Gene Therapy

- Transport gene product on ice into mixing area
- Swab all surfaces of BSC with 10% bleach solution followed by 70% alcohol
- Line empty sharps container with a leakproof biohazard bag

DeCederfelt, et al. *AJHP* 1997;54:1604-10

Pharmacy and Gene Therapy

- Compounded product is usually very time sensitive
- Decontamination of BSC should be repeated
- Everything utilized in the process should be autoclaved for at least 15 minutes

DeCederfelt, et al. *AJHP* 1997;54:1604-10

Pharmacy and Gene Therapy

- Preparation methods
- All gene therapy preparations require double check
- Supply disposal
- Delivery to treatment area

Univ . Of Kentucky Pharmacy Policy PH-10-04

Pharmacy and Gene Therapy

- Decontaminate BSC with current, Infection Control approved, anti-viral disinfectant prior to & after each use
- Do not use BSC for 1 hour after cleaning

Univ . Of Kentucky Pharmacy Policy PH-10-04

Pharmacy and Gene Therapy - UK

- Biological safety officer
- Task force / working party
- Genetic modification safety committee
- Standard operating procedures

Simpson J. Pharmaceutical Journal 2003;271:127-30

Pharmacy and Gene Therapy - UK

- Handling
- Storage
- Cleaning
- Dispensing
- Labelling
- Operators
- Transport
- Waste Disposal
- Spillage

Simpson J. Pharmaceutical Journal 2003;271:127-30

Pharmacy and Gene Therapy - UK

- Questionnaire regarding UK pharmacist knowledge
- Majority expressed concerns over safety of gene therapy
- Majority wanted pharmacists involved in process

Yousif S, Gorecki DC. Pharmaceutical Journal 2004;272:159-162

Pharmacy and Gene Therapy - UK

- Genetically Modified Organisms (GMO) Regulations
  - 'Contained Use'
  - 'Deliberate Release'
  - Class 1 to Class 4

Beaney AM. *Quality Assurance of Aseptic Preparation Services.* 2006

Pharmacy and Gene Therapy - UK

- Regulatory requirements
  - Regulation 17
  - Regulation 18 and Schedule 8

Beaney AM. *Quality Assurance of Aseptic Preparation Services.* 2006
Health & Safety Executive website:
http://213.212.77.20/biosafety/gmo/index.htm

Pharmacy and Gene Therapy - UK

- Facilities
  - Not normally appropriate to handle these products in cytotoxic facilities
- Documentation
- Labeling
- Training

Beaney AM. *Quality Assurance of Aseptic Preparation Services.* 2006

Pharmacy and Gene Therapy - UK

- Aseptic processing
- Cleaning
- Storage
- Transport
- Waste disposal
- Spillage

Beaney AM. *Quality Assurance of Aseptic Preparation Services.* 2006

Conclusions

- Use of gene therapy products will continue to increase over the next decade
- Laboratory practice guidelines are not sufficient to meet the needs of pharmacies working with these agents

Conclusions

- Pharmacy guidelines for preparation of gene therapy products are necessary
  - Vector classification schema
- Appropriate training of pharmacists is critical

Questions

?

References

- Smith TJ. Gene therapy: Opportunities for pharmacy in the 21st century. *Am J Pharm Education*. 1996;60:213-15
- DeCederfelt HJ, et al. Handling of gene-transfer products by the National Institutes of Health Clinical Center pharmacy department. *Am J Health-Syst Pharm*. 1997;54:1604-10

References

- Center for Biologics and Evaluation and Research. *Guidance for Human Somatic Cell Therapy and Gene Therapy*. Bethesda, MD. 1998 http://www.fda.gov/cber/gdlns/somgene.pdf
- Roth RI and Fleischer NM. *Gene therapy:* Applications to pharmacy practice. *JAPhA*. 2002;42(5):692-98

References

- Simpson J and Stoner NS. Implications of gene therapy for hospital pharmacists. *Pharmaceutical Journal*. 2003;271:127-130
- Yousif S and Górecki DC. Are pharmacists ready for gene therapy? *Pharmaceutical Journal*. 2004;272:159-62

References

- University of Kentucky Hospital Department of Pharmacy Policy on Gene Therapy 10/26/2005. http://www.hosp.uky.edu/pharmacy/departpolicy/PH10-04.pdf

References

- Simpson J. Progress in gene therapy – are hospital pharmacies the next barrier? *Hospital Pharmacist*. 2006;13:266
- Beaney AM. Quality assurance of aseptic preparation services. 4th edition. Appendix 6: Gene therapy. London: The Pharmaceutical Press; 2006