**Mission**
- To provide to the Weill Cornell, Cornell Ithaca and associated centers the infrastructure to carry out basic, translational and clinical research utilizing gene transfer for therapeutics and vaccines

**Gene Therapy**
- Human genome
- Therapeutic gene
- Target organ
- Delivery vehicle

**Vectors as Drug Delivery Vehicles**

<table>
<thead>
<tr>
<th>Vector</th>
<th>Gene expression</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasmid ± liposome</td>
<td>Low</td>
<td>Transient</td>
</tr>
<tr>
<td>Retrovirus</td>
<td>Moderate</td>
<td>Persistent</td>
</tr>
<tr>
<td>Lentivirus</td>
<td>Moderate</td>
<td>Persistent</td>
</tr>
<tr>
<td>Adeno-associated virus</td>
<td>Moderate</td>
<td>Persistent</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>High</td>
<td>Transient</td>
</tr>
</tbody>
</table>

**Example of Gene Transfer Adeno-associated Virus Vectors**

**Vector Core**
- The vector core aims to provide the Cornell community with access to gene transfer vectors primarily for in vivo gene therapy experiments.
- It also serves as an educational facility and will train personnel in the relevant technology.
- The core is committed to adopting innovative technology developments in the field and introducing new applications.
- The vector core has a fully equipped and supported laboratory and cell culture spaces, a training program, protocols and the biological materials required for making adenoviral, adeno-associated virus, retrovirus, lentivirus, plasmid gene transfer and stable cell banks for therapeutics and vaccines

**Gene Therapy Clinical Development**

**GMP Core**
- Produces clinical grade adenovirus, adeno-associated virus and plasmids
- ~2,400 square foot GMP facility, plus associated office space and non-GMP laboratory space

**Environmental Monitoring is Performed to Ensure Product Quality**
- Real-time 24/7 monitoring of critical facility parameters by wireless R&D Scientific Datatron system
- Data accessible via the internet and in QA/QC office in the facility
- System contacts GMP personnel by phone to notify of parameters out of specification
- All data is stored permanently, locally, and at R&D Scientific
- In addition to Datatron there is weekly assessment of viable and non viable particles

**GMP Technicians in the Facility Being Observed by Supervisor**

**Production Requirements Under Good Manufacturing Practice**
- Document Control (SOPs, Batch Records, etc)
- Tracking of Materials
- Flow of Materials/Personnel
- Stability Testing
- Test Parameters and Specifications
- QC Testing
- Environmental Monitoring
- Personnel Training

**Example of Process Control Facility Flow of Personnel**
- Personnel flow within the production facility. The arrows on the map of the facility indicate the allowed direction of personnel flow. These rules are enforced by SOP and hardware. Doors within the facility have no hardware on the side of forbidden entry to prevent SOP violation.

**Mandatory Record Keeping Production Data Records**
- Released upon QA/QC Approval
- Assures the use of the most current revision
- Records are modular
- Can be easily varied based on project needs
- Nonconformance Report: Documents non-compliance with standard operating procedures and captures a risk analysis to product safety and quality
- Change Request Approval: Revision of an existing or implementation of a new process is controlled by a change control mechanism. If the change is major, validation may be required.
- Corrective and Preventative Action (CAPA): Serves to identify the root cause of systemic problems and implement a corrective or preventative action

**Vector Quality Control**
- Safety testing for gene therapy products are no different from other biopharmaceuticals.
- However, there are unique challenges and certain tests are necessary
- Characterization of the Cell Lines Used
- Usually a two-tier system of master and working cell banks which must be validated before use.
- In-process Testing
- Intermediate products (i.e. cell harvests) are tested for mycoplasma, bioburden, and adventitious viruses
- Lot Release
- Before release the final product is assessed for safety and characterized. Safety testing includes sterility, endotoxin, and residuals testing. Final product characterization includes tests for identity, purity, potency, titer, and infectivity

**Example of Lot Release/Certificate of Analysis**

**Summary of Ongoing and Complete GMP Manufacturing**

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