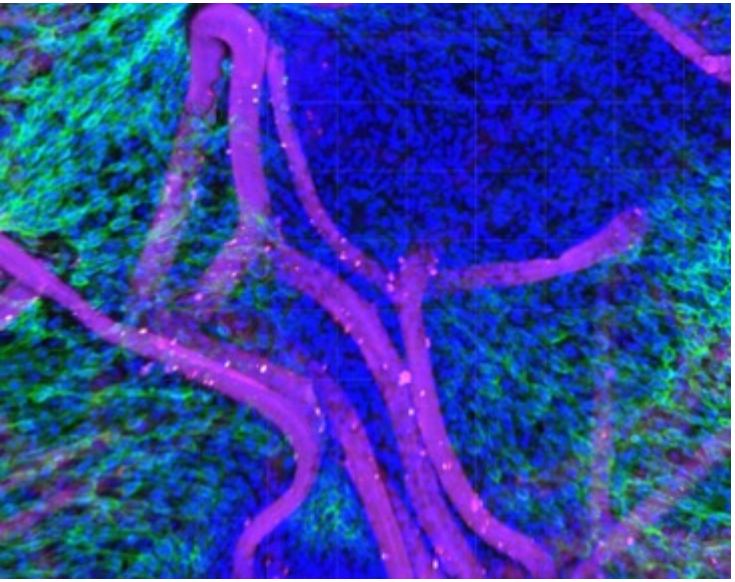
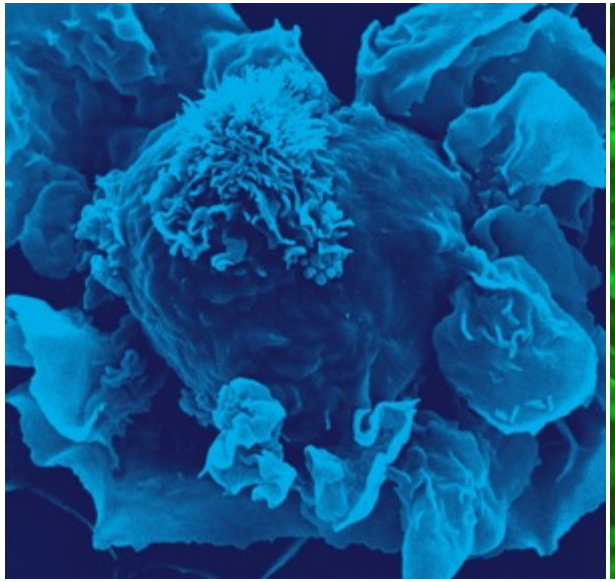
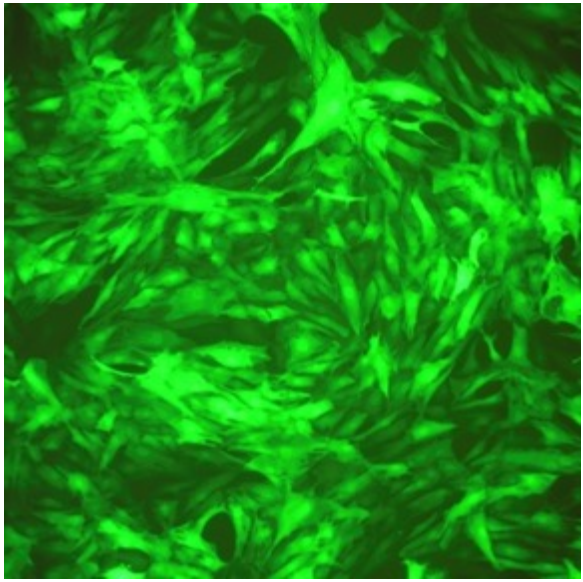
MAYO CLINIC

IMMUNE, PROGENITOR, AND CELL THERAPEUTICS (IMPACT)

Contract Manufacturing at an Academic Medical Center

Allan B. Dietz, Ph.D.

FACT Webinar
November 2020

Contract Manufacturing at Mayo Clinic

- CM for phase I, II and III trials
- Multiple companies
- >350 manufactured products
- >125 patients

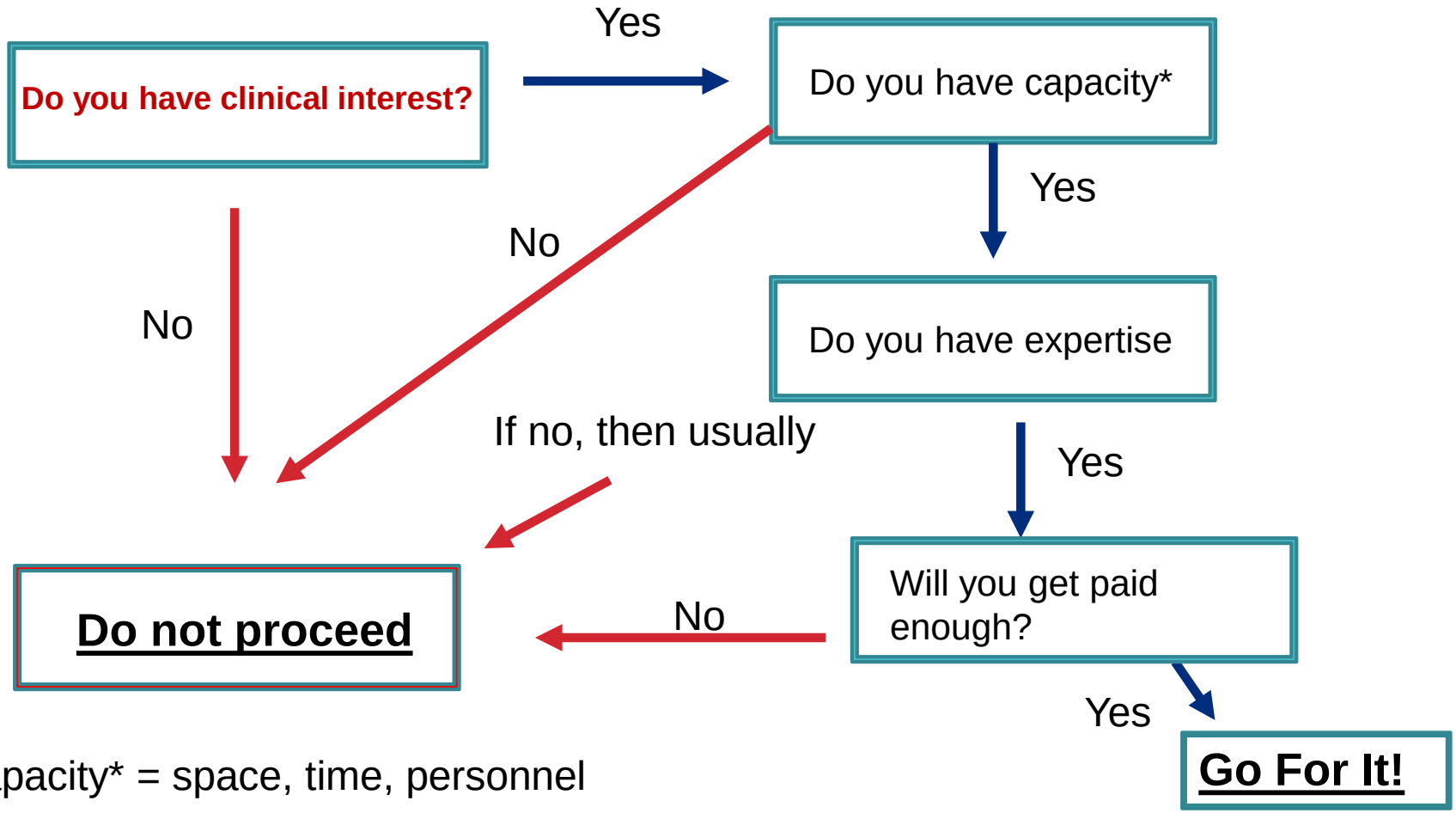
Dendreon

Contract Manufacturing		
Activity	Patients	Total performed
Collection	130	356
Manufacture	127	353

Contract manufacturing

- What is it?
  - Trading your time, expertise, space and equipment
- Why would you do this crazy thing?
  - $
  - To fill gaps that occur in production runs/to get facility to capacity
  - To gain some expertise
  - To “fit” new product into a clinical program

Decision Matrix for Contract Manufacturing



capacity* = space, time, personnel

Considerations in regards to contract manufacture…capacity

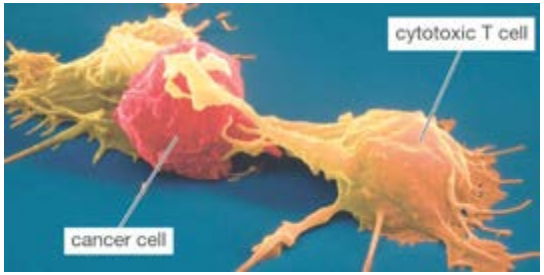
- Capacity calculations
  - Understand prioritization
    - Time is money for companies
  - Space
    - Dedicated clean room?
  - People and training
    - Train the trainer?
  - Expertise
    - Does the project need any development (validations, new SOPs, etc.)?

Considerations in regards to contract manufacture…capacity

- How to decide if you have capacity?
  - Get as much detail as you can
    - Review SOP, data, requirements
  - Try to estimate gaps between what they need and what they have
    - Could be zero…could be a lot
  - BE REALISTIC on time
    - It will probably take more time than you think

Capacity, budget, and time

- The calculus used to understand your capacity (infrastructure, people, development needs etc.) is the basis you use to start estimating both
  - Time
  - Budget



- Both of which (if they are excessive) will be non-starters for the company…

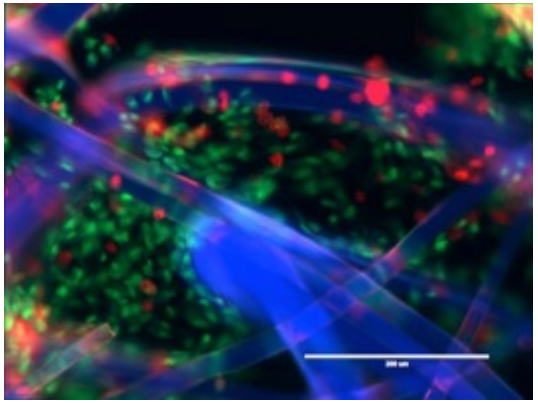
Agreements

- You have a feel for the time and budget AND you think you have capacity
- Now time to figure out how you work together

- Technical Agreement
- Quality agreement
- *(Intellectual property, confidentiality, liability are not discussed here but should be addressed somewhere)*

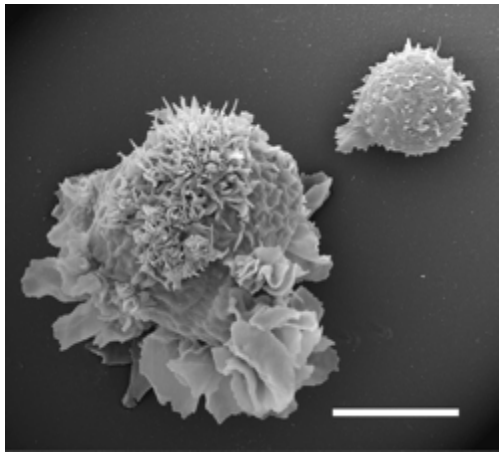
Technical Agreement Part 1

- What you are going to do?
  - How many runs
  - What release tests
  - Extra work if necessary (development, new release assays, equipment validation etc.)



Technical Agreement Part 2

- What you need
  - List of SOPs (Document Matrix)
  - List of Critical Materials
  - Process specific equipment



Quality Agreement

- The quality agreement describes who is responsible for the quality aspects of manufacturing
  - Ultimately – the Sponsor is responsible, however, *how they do that job via the interaction with the CRM* is what is outlined in the QA

Quality Agreement

- Parts of a QA
  - Monitoring plan
    - What the Sponsor considers sufficient information to meet their regulatory requirements for example:
      - *Pre-audit*
      - *Review CoA*
      - *Scheduled batch record review*
    - Anything else is transferred to fall under typical CRM quality unit responsibilities
  - Communication plan

Quality Agreement

- Parts of a QA - the Communication plan
  - What are you communicating?
  - When will it take place?
- Examples…
  - Product fails release testing - Immediate
  - Minor event during processing (verifier signature missed on one step of SOP – within 5 working days
  - Courier was late for scheduled pick up – at monthly meeting
- The Document matrix and critical materials list in TA are reference points for communication
  - Things on that list fall to higher urgency in communication

Timing and budgets

- Proposal hits your desk…
  - Review for capacity, expertise, time
  - Do your best to estimate time and resource requirements for BOTH the Quality and technical agreements
  - Bid out in two parts; quality agreement work and technical work

They accept the bids…

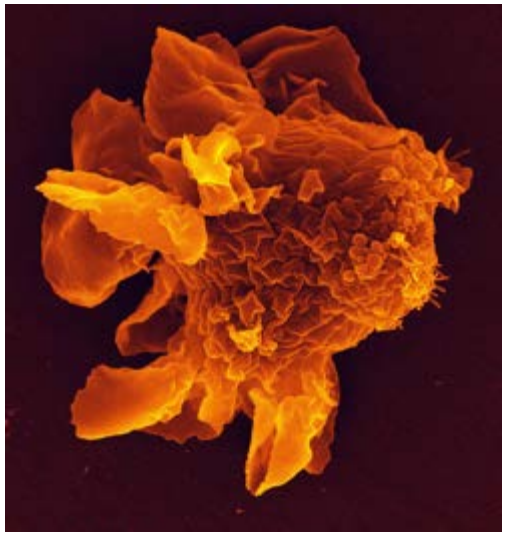
They accepted the bids – PART 1

- Start the QA agreement process
  - Get list of critical materials
  - Get a list of SOPS in document matrix
  - Agree on communication matrix
  - Get required equipment

- Once completed with the QA part – then should be good to go on the technical agreement
- Should be able to provide validated test runs of process – IND filings

They accepted the bids – PART 2

- Initiate the TA agreement
  - With the QA done, this should be easy
  - Manufacture according to plan reviewed and approved SOP
  - Refer to the QA for communication/reporting issues
  - MEET THE TIMING MILESTONES



The final steps

- Close out
  - Make sure the close out process is included in the agreements
  - Final transfer and sign off of all documents
  - Retained product transfers

IT'S THAT SIMPLE