Session 3: Establishing a sequencing laboratory

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Key areas:

- Understanding your goals
- Laboratory infrastructure
- Logistics
- Quality control

Understanding your goals

Understanding your goals

- You overall aim will influence how you set up, so consider your research/diagnostic questions:
  - What are you aiming to sequence (e.g. human, bacterial, viral, fungal DNA?)
  - What data do you want to obtain? (e.g. just species level? Metagenomics? Detailed SNP data?)
  - Will the laboratory be used for (academic) research, routine diagnostics, as a service, or a combination of the above?
  - How many different research questions do you have? (do you need a more flexible sequencing system?)
  - Will your sequencing laboratory be used by others too? (versatility)

Understanding your goals

- Throughput
  - Consider how many samples you may plan to run per day, week, month and year. Is this likely to change (increase or decrease) over time?
  - Can you batch samples (making it more cost effective), or is it necessary to run samples as they come in?
  - If you are planning high throughput, consider automated systems (e.g. extraction and library prep robots, automated gel electrophoresis machines)

Understanding your goals

- How flexible are you planning to be for the future?
  - Do you need your sequencing system to work for multiple different uses?
  - Is it worth investing in multiple systems?
  - If you want to make it a service, have you considered accreditation etc.?

Understanding your goals

- Consumables
  - Are there certain platforms (equipment and reagents) that are easier to get hold of in your country?
  - Consider the costs of additional reagents (some sequencing platforms, or kits within platforms, require a number of expensive extra reagents)
  - Consider the quality control equipment you might need (e.g. fluorometers, automated gel electrophoresis machines)

Understanding your goals

- Cost and sustainability
  - How long do you envisage needing the sequencing laboratory?
  - Have you considered the yearly running costs? (costs per sample, maintenance, staffing costs etc.)
  - Is the laboratory (and costs) going to be incorporated into a programme (e.g. national diagnostics)?
  - If you are relying on grants etc. to keep it going, how will you confirm funding?

Laboratory infrastructure

Laboratory infrastructure

- Internet
  - You will need to consider the speed and reliability (and this may incur costs)
  - Some sequencing platforms (e.g. Oxford Nanopore's MinION) require internet to start a sequencing run, others (e.g. Illumina) don't, so internet reliability might be important
  - Bioinformatic analysis can rely heavily on browser and server based systems, so fast internet speeds can be vital to a good working service

Laboratory infrastructure

- Power
  - Do you frequently experience power surges, load shedding or blackouts?
  - Sequencing equipment needs a constant power supply for hours or days
  - Will the sequencing run cut out completely if power is lost (e.g. could you run a MinION on a battery powered laptop as a back up power supply, or would you need to run a mains powered MiSeq?)
  - How is your power supply backed up? Do you have generators and uninterruptable power supplies (UPS)?

Laboratory infrastructure

- Automation
  - Would the cost of implementing automation be cheaper than hiring staff in the long run?
  - Would automation be better for quality control if you are doing routine diagnostics and/or providing a service?
  - Do you have the space in your laboratory for these (often very large) pieces of equipment?

Laboratory infrastructure

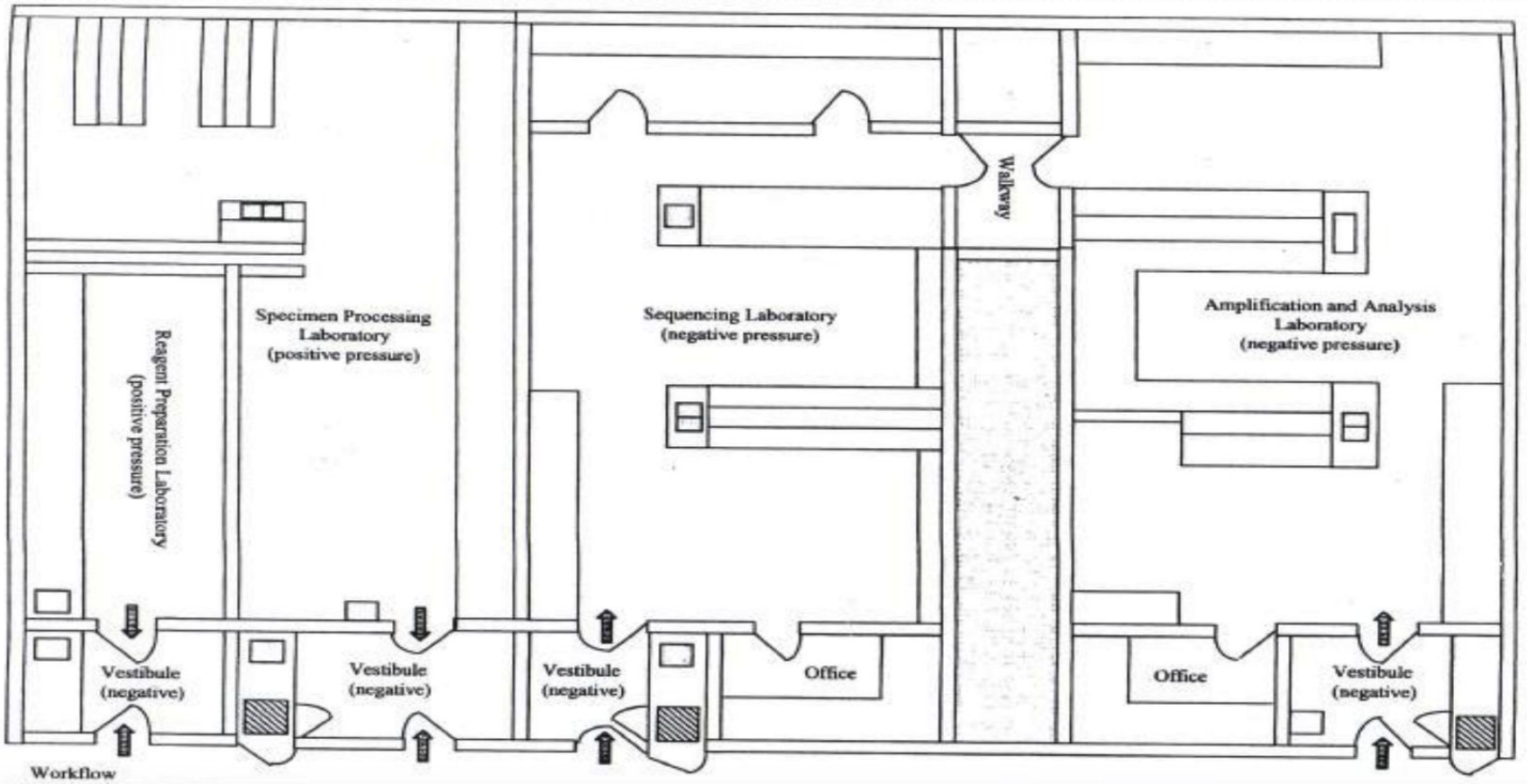
- Biosafety
  - Will you be extracting the DNA, or would you expect other groups to provide the DNA for you?
  - What hazard group level samples will you be sequencing?

Laboratory infrastructure

- Physical space
  - Have you made a floor plan? E.g. considered the footprint of all of your pieces of equipment, not just the sequencer, but fridges, freezers, robots, work space etc.?
  - Are you sharing your workspace with any other groups?
  - Do you have enough space for the number of expected staff members to work comfortably?
  - Ideally, you would need at least 3 rooms (DNA extraction, library preparation and Sequencing) and uni-directional workflow to prevent contamination

Laboratory Design Example 1

Mitchell P. S. et al. Nucleic Acid Amplification Methods: Laboratory Design and Operations, 2004, In "Molecular Microbiology: Diagnostic Principles and Practice, edited by D. H. Persing et al" 99. 85-93.



Laboratory infrastructure

- Computing requirements and data storage
  - Some platforms have built in computers (e.g. GridION, MK1C, Illumina machines) but others require a computer/laptop to run them. These will need to be powerful (consider GPU rather than CPU)
  - Sequencing outputs huge volumes of data (a single run can be hundreds of GB)
  - Where will you store the data? Hard drives (not ideal for long term storage), server or cloud-based?
  - Accessibility of data (ease of access and also GDPR)
  - Long term storage (save larger raw data, so can be re-analysed later on or just fastq? How long will you keep it for?

Logistics

Logistics

- Shipping and customs
  - Some items (e.g. Oxford Nanopore flow cells have a 3 month warranty)
  - How long (and reliable) is the customs/importation process?
  - Do you have reliable suppliers for the platform(s) you want to use? E.g. is there an in-country supplier, or would you have to get it from overseas?
  - How long does it take for those items to be delivered? Are there often supply chain issues?
  - Do you have back up or alternative reagents if there are supply chain issues?

Logistics

- Storage
  - If there are shipping delays, do you have enough storage space (room temperature, fridge and freezer) to store enough reagents to cover the backlog?
  - Do you have an adequate storage and ordering system to maintain constant supplies?

Logistics

- Maintenance
  - Are there in-country Nanopore/Illumina/PacBio etc. maintenance teams available to service and/or repair your equipment when needed?
  - If not, how will this be solved?
  - Do you have responsive access to online customer service/support teams?
  - Do you have a back up plan if a machine breaks and you can’t sequence for days/weeks/months?

Quality control

Quality control

- Staff training
  - Will you provide staff training for all steps of sequencing? Or have individual staff working on different parts?
  - Have you considered the cost of staff training? (e.g. online bioinformatics courses, in-person events)
  - Consider staff retention (will you have to train people again next year?)
  - GCP and GCLP and other QC training?
  - How will you record staff training?
  - Will you employ a quality manager?

Quality control

- Quality management/documentation
  - Audits (vertical, horizontal, in-house, external)
  - SOPs for each part of the process
  - Policy documents
  - Risk assessments

Quality control

- Accreditation
  - Are you planning to provide a service?
  - Could accredit the whole laboratory, or individual protocols etc.
  - It is costly and time consuming to achieve (and maintain) accreditation
  - Consider SLMTA/SLIPTA

Quality control

- LIMS
  - Many different LIMS systems for different processes/laboratory sizes
  - Consider the long-term costs vs savings on staff time when implementing

Group activities

Participants will be put into 6 groups:

Activity 1: Each group will be be tasked with setting up a sequencing laboratory scenario. You will be given a worksheet with different parts of the set up, you must decide in your group what would fit best for your scenario

Activity 2: You will be given a scenario and information about different sequencing platforms. You must decide within your group which is the most appropriate and why.

Activity 3: Each group will be given a sequencing set up ‘problem’ and must come up with a solution.