A Quick Introduction to

DIAMOND

MAKING DIAGNOSIS PERSONAL

During the COVID Pandemic

A Quick Introduction to DIAMONDS MAKING DIAGNOSIS PERSONAL

SECTION 1: PROJECT OVERVIEW

Official Title

Diagnosis and Management of Febrile Illness using RNA Personalised Molecular Signature Diagnosis

Overall Objective

Derivation of a host gene expression-based test that can diagnose multiple conditions simultaneously at the point of testing.

Concept

- Different genes are 'switched on' or 'switched off' (gene expression) in response to different conditions (even when clinically similar).
- By using a single test that measures expression of a modest number of genes (50-150) a broad range of infectious and inflammatory conditions can be accurately identified.

The Role of DIAMONDS in the COVID Pandemic:

- RNA expression has potential to help explain immunopathogenesis, and identify predictive markers
- DIAMONDS has CMO approval as national priority project to address COVID-19, as we are well-placed to tackle these questions:
    - Is there a host-based signature for COVID-19?
    - Can it discriminate pure SARS-CoV-2 disease from coinfections, for instance with bacteria?
    - Do different clinical manifestations have distinct host signatures, for instance, mild vs severe; inflammatory vs uncontrolled viral disease?
    - Can we use a host signature to detect and understand the SARS-CoV-2 Inflammatory Syndrome?
    - Might a gene expression signature predict progression?

DIAMONDS Priorities During the COVID Pandemic

- Urgent recruitment of adults and children with all presentations related to COVID, including:
    - Suspected/proved COVID19.
    - SARS-CoV2 Inflammatory Syndrome.

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SECTION2: RECRUITMENT, CONSENT & DATA COLLECTION

Inclusion Criteria

- Patients of ALL ages.
- All presentations that may be related to COVID, including:
    - Mild (not admitted).
    - Moderate (admitted, but not to intensive care).
    - Severe (on CPAP/invasive ventilation, or fatal cases).
    - Suspected SARS-CoV-2 Inflammatory Syndrome.

Exclusion Criteria

- Patients who do not give consent.
- Patients where an RNA sample was not taken.

Consent

- Who can give consent?
    - Consent by parents and guardians under 16 years
    - Assent by child if appropriate
    - Consent by patient aged 16 and over

- Deferred consent
    - First set of research bloods samples may be taken without consent.
    - No further samples taken until consent obtained.

- Modes of consent, in decreasing order of preference:
    - Written – where possible as first choice.
    - Electronic - by text to study mobile, or email; eg photo of consent form
        - PI to countersign consent form.
    - Verbal consent – eg for suspected SARS-CoV-2; no need for paper forms.
        - verbal consent confirmed by signature from a second staff member.
        - verbal consent validated with consenter by PI countersignature.

Data Collection

- Complete COVID Case Record Form (CRF): click here
- Web-accessible eCRF.
    - Database manager can issue login/passwords for the database:
        - Tisham De - tisham.de08@imperial.ac.uk.

- Study number will be automatically generated by database.
- Search patient identification log first to find out if patient has already been recruited.
- Use previously given study number with next episode number.
- Re-consent only if patient did not previously agree to more samples/data being taken.

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SECTION 3: SAMPLE COLLECTION

Timepoints

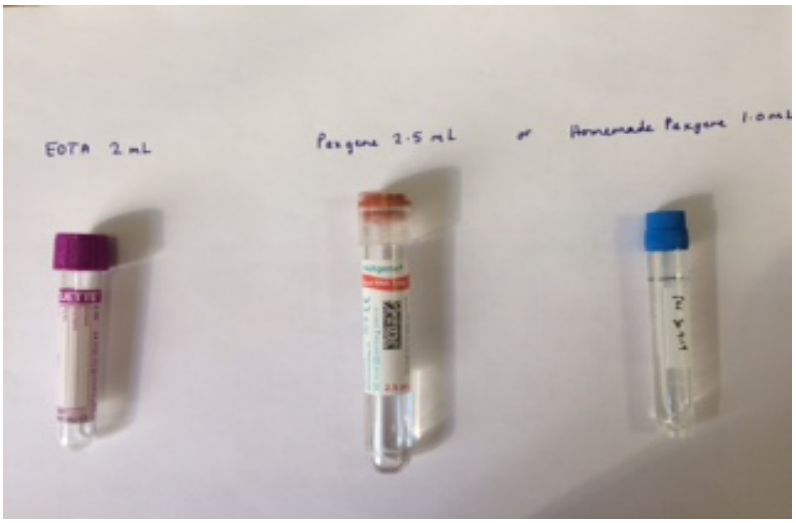
- Research samples to be taken at 3 timepoints

- Timepoint 1:
  - As early as possible in illness.
  - Ideally on presentation to ED, collected alongside 1st blood draw.
- Timepoint 2:
  - With the 1st clinically indicated blood draw after 48 hours, or later (7-14 days) in patients with a slow expected time course of recovery.
- Timepoint 3:
  - After convalescence
  - With the first clinically indicated flood draw after recovery from acute illness
  - E.g. First outpatient follow-up visit

- Not all research samples have to be taken with clinical samples, e.g.:
  - Patients with central access lines, where blood can be drawn painlessly, without needle puncture.
  - Patients where consent is obtained for research-indicated testing.

Samples (see pictures below)

- Blood samples in order of priority:
  - PAXgene.
  - EDTA – to be separated into whole blood, plasma and pellet aliquots.
  - Serum (adult patients with larger samples only).
- Throat swab / Nasopharyngeal aspirate:
  - Collect in eNAT tube (inactivated viruses).



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SECTION 4: SAMPLE HANDLING

Standard Operating Procedures

- Can be found in the DIAMONDS Box folder
  - For access, PI should contact Cristina Romano (c.romano@imperial.ac.uk)
- Any concerns/edits, email Rachel Galassini (r.galassini@imperial.ac.uk) & Victoria Wright (v.wright@imperial.ac.uk).

Tube and Storage Box Labelling

- Specimen Collection Tube
  - **Unique Subject ID (USID)**
  - **Date, Time point, type of sample**

- Sample Aliquot Tube
  - **Unique Subject ID**
  - **Date of collection, time point**,
  - **Type of sample**, aliquot number, volume

- Sample Storage Box
  - **Project ID, Centre ID, box number, sample type, date,** (shipment number when necessary)

- Online sampling database being created to generate labels and log and track samples.

Research Samples

- PAXgene
  - 1ml if using "home-made" PAXgene tube, 2.5ml if using 10ml PAXgene tube.
- EDTA
  - 220 or 450 depending on volume of blood drawn.
- Smart Tube
  - If enough blood drawn, ≥2ml aliquoted directly from EDTA vacutainer.
- Plasma
  - 2ml or 4ml depending on volume of blood drawn
- Cell Pellet
  - 2ml or 4ml depending on volume of blood drawn
- Serum
  - 4ml, only if enough blood after filling PAX and EDTA vacutainer.
- Throat Swab
  - eNAT kit preferred as it inactivates viruses.

SECTION 5: CONTACT INFORMATION

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Project Management Office:

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Patient/Phenotyping:

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Database:

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Ethics, Regulatory, Supply Ordering:

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Laboratory Sample Handling

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