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Sequencing in Suspected Infection (SePSI)

Submission date 29/10/2015	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 03/11/2015	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 21/05/2021	**Condition category** Signs and Symptoms	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims
The Illumina MiSeq machine is able to detect the genetic material of bacteria, viruses and fungi directly from clinical samples such as blood, urine and throat and nose swabs. This study aims to find out whether genome sequencing of clinical samples using the Illumina MiSeq machine is useful in the investigation of patients presenting to hospital with fevers and suspected infection.

Who can participate?
Adult patients presenting to Southampton General Hospital with a fever (febrile).

What does the study involve?
Blood samples, throat and nose swabs, urine (and stool if diarrhoea is present) are taken and stored for analysis at a later date with the Illumina MiSeq sequencing machine. Information from patients is also collected as they enter the study and again at follow up 4 weeks later, to better understand the sequencing results. The potential impact of the sequencing results is assessed by determining the number of additional diagnoses which were made using sequencing compared with standard tests. Fifty healthy volunteers are also recruited to allow us to understand which organisms detected by sequencing in febrile patients are actually making them ill and which are 'bystanders' and are also present in health.

What are the possible benefits and risks of participating?
We aim to use the results of this small study to plan a larger and more detailed study of this technology in the future. The potential benefits of participating are that a diagnosis that would otherwise not been obtained will be made. However, the usefulness of next generation sequencing in this context is not known; this study aims to find out whether next generation sequencing is a clinically useful test in patients presenting with undifferentiated febrile illnesses. The risks include minor discomfort of throat and nose swabbing and bruising and discomfort associated with blood sampling. There is a small possibility of detecting a previously undiagnosed blood borne virus, but all febrile patients will be offered routine testing for hepatitis B, C and HIV as part of standard care and this is fully explained in the participant information sheet, consent and protocol.

Where is the study run from?
Southampton University NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
November 2015 to November 2016.

Who is funding the study?
Southampton Respiratory Biomedical Research Unit (UK)

Who is the main contact?
Dr Rebecca Houghton

Contact information

Type(s)
Scientific

Contact name
Dr Rebecca Houghton

Contact details
LB22 Registrar’s office, Level B PHE laboratory
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Southampton General Hospital
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Southampton
United Kingdom
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Additional identifiers

Protocol serial number
2.0

Study information

Scientific Title
The use of unbiased next generation sequencing for pathogen detection in adults hospitalised with acute undifferentiated febrile illness and suspected infection: an observational pilot study (SePSI)

Acronym
SePSI

Study objectives
The use of unbiased next generation sequencing will improve the proportion of patients with acute undifferentiated febrile illness (AUFI) achieving a credible diagnosis, compared to standard diagnostic testing.

Ethics approval required
Old ethics approval format

Ethics approval(s)

South Yorkshire Research Ethics Committee, 15/10/2015, ref: 15/YH/0429

Study design
Prospective observational controlled single-centre pilot study

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Undiagnosed undifferentiated febrile illness in adults

Interventions
Written, informed consent. Pregnancy testing with consent for women of child-bearing potential.

Febrile participants:
The acquisition of additional nasopharyngeal viral swabs in viral culture medium, an aliqout of urine (15 ml) and serum and whole blood sampling (total volume of 20 ml on recruitment and 20 ml at follow up 28 days -/+ 14 days following the onset of illness) for later unbiased next generation sequencing. These samples will be taken in addition to those required by the clinical team for routine clinical care. Detailed clinical data including travel, medical history and medication will also be obtained.

Healthy controls:
The acquisition of nasopharyngeal viral swabs in viral culture medium, an aliqout of urine (15 ml) and serum and whole blood sampling (total volume of 20 ml) on recruitment. Clinical data regarding past medical history, medications and travel. No further visit will be required.

Methodology:
Febrile participants will be identified from the comprehensive emergency department and acute medical unit electronic admission lists within 72 hours of presentation. Participants may also be identified and referred by the inpatient infectious diseases team.
Healthy volunteers will be recruited using a poster approved by the ethics committee.
Fully GCP trained study doctors and nurses will approach participants in a non-coercive manner and discuss the details of the trial and offer written information. If the individual consents to recruitment, formal written consent will be obtained and the samples as listed above will be taken and stored in an anonymised format.

Intervention Type
Other

Primary outcome(s)
Proportion of patients with a credible diagnosis made by NGS compared with standard diagnostic testing

Key secondary outcome(s))
1. Sensitivity and specificity of NGS in patients where a clinically credible diagnosis was made using standard current investigations
2. Actionable diagnoses made (i.e., a potential change in management was indicated if NGS

result was known by the clinical team in real time)
3. Potential impact of NGS results on antimicrobial use and course duration
4. Assessment of the healthy human microbiome in different body compartments as assessed by NGS

Completion date
31/12/2017

Eligibility

Key inclusion criteria
Febrile participants:
1. Aged 18 years or over
2. Has the capacity to give informed, written consent and is able and willing to adhere to the study procedures
3. Is a patient in Southampton General Hospital Acute Medical Unit or Emergency Department OR is under the care or advice of the inpatient infectious diseases service
4. Can be recruited to the study
4.1. Within a 72-hour period of first triage by ED staff OR
4.2. Within a 72-hour period of arrival on AMU (if admitted directly to AMU)
4.3. Has an acute febrile illness with a documented fever ≥38°C, OR a history of fever in the preceding 72 hours
5. Has a duration of illness less than or equal to 21 days
6. Has an illness lacking localizable or clear organ-specific clinical features (as determined by the investigators), including but not limited to:
6.1. Pneumonia (as defined by new radiological consolidation)
6.2. Urinary tract infection
6.3. Cellulitis or other skin and soft tissue infections
6.4. Septic arthritis
6.5. Infected prosthetic material
6.6. Pyogenic spondylodiscitis
6.7. Meningitis
7. Has an illness lacking a clear non-infectious aetiology

Healthy volunteers:
1. Aged 18 years or over
2. Has the capacity to give informed, written consent and is able and willing to adhere to the study procedures
3. For women of childbearing potential, has a negative pregnancy test
4. Has been well with no symptoms of significant illness (including; fever, chills, sweats, myalgia, arthralgia, malaise, weight loss, cough, chest pain, rhinorrhoea, sore throat, abdominal pain, diarrhoea, dysuria, urinary frequency, haematuria, severe headache, collapse or seizure) in the past 14 days
5. Normally fit and well with no significant medical co-morbidity (including chronic cardiovascular, respiratory, renal, hepatic or neurological illness, diabetes mellitus, malignancy and others at discretion of the investigators)
6. Not immune compromised (as defined above)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Febrile participants:
1. Patients not fulfilling inclusion criteria
2. A decision to palliate the patients symptoms taken by the treating clinicians
3. Declines collection of clinical specimens
4. Immune compromised as defined by;
4.1. HIV infection with a CD4 count of less than 200 cells/µl
4.2. Any primary immunodeficiency
4.3. Current or recent (within six months) chemotherapy or radiotherapy for malignancy
4.4. Solid organ transplant recipients on immunosuppressive therapy
4.5. Bone marrow transplant recipients currently receiving immunosuppressive treatment, or who received it within the last 12 months
4.6. Patients with current graft vs host disease
4.7. Patients currently receiving high dose systemic corticosteroids (equivalent to ≥ 40 mg prednisolone per day for ≥3 week in an adult), and for at least three months after treatment has stopped
4.8. Patients currently or recently (within three months) on other types of immunosuppressive therapy.
5. The investigator feels that patient should not be enrolled (i.e. investigator discretion)
Involvement in other research trials is not necessarily an exclusion criterion. Concurrent, prior or subsequent enrolment in an observational study is not expected to be an exclusion criterion, except at the discretion of the PI.

Healthy volunteers:
1. Not meeting inclusion criteria
2. Receiving antibiotics or antiviral in the last 2 weeks

Date of first enrolment
09/11/2015

Date of final enrolment
09/11/2017

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Southampton University NHS Foundation Trust
Southampton General Hospital
Tremona Road
Southampton
Southampton
United Kingdom
SO16 6YD

Sponsor information

Organisation
University Hospital Southampton NHS Foundation Trust (UK)

ROR
https://ror.org/0485axj58

Funder(s)

Funder type
Government

Funder Name
Southampton Respiratory Biomedical Research Unit

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No