Infectious Disease Biomarkers

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Frontiers Meeting

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Considerations and Goals

- Screen all 500,000 UKB participants for:
  - Prior exposure to pathogens
  - Carriage of pathogens
- Focus on pathogens suggested to be associated with chronic disease pathogenesis
- Use antibody in blood as a marker of exposure / infection
- Plan to screen a subset on at least two timepoints

Possible Methodological Aims

- Perform the largest seroepidemiology study ever undertaken
- Test for associations between infection carriage / exposure and chronic disease
- Overlay human genotype data to help understand:
  - Chronic disease pathogenesis
  - Infectious disease susceptibility

Pathogen List

Pathogen
Herpes simplex virus-1 (HSV-1)
Herpes Simplex virus-2 (HSV-2)
Varicella zoster virus (VZV)
Epstein-Barr virus (EBV)
Cytomegalovirus (CBV)
Human herpesvirus-6 (HHV-6)
Human herpesvirus-7 (HHV-7)
Karposi sarcoma-associated herpesvirus (KSHV/HHV-8)
Hepatitis B virus (HBV)
Hepatitis C virus (HCV)

Pathogen
Human immunodeficiency virus (HIV)
Human T-cell lymphotropic virus (HTLV-1)
Human papillomavirus (HPV)
Polyomavirus JC/BK
Merkel cell polyomavirus
Borrelia burgdorferi
Chlamydia trachomatis
Helicobacter pylori
Staphylococcus aureus
Toxoplasma gondii

Proposed Associations with Cancer

Pathogen
Herpes simplex virus-1 (HSV-1)
Herpes Simplex virus-2 (HSV-2)
Varicella zoster virus (VZV)
Epstein-Barr virus (EBV)
Cytomegalovirus (CBV)
Human herpesvirus-6 (HHV-6)
Human herpesvirus-7 (HHV-7)
Karposi sarcoma-associated herpesvirus (KSHV/HHV-8)
Hepatitis B virus (HBV)
Hepatitis C virus (HCV)

Pathogen
Human immunodeficiency virus (HIV)
Human T-cell lymphotropic virus (HTLV-1)
Human papillomavirus (HPV)
Polyomavirus JC/BK
Merkel cell polyomavirus
Borrelia burgdorferi
Chlamydia trachomatis
Helicobacter pylori
Staphylococcus aureus
Toxoplasma gondii

Proposed Associations with Cardiovascular Disease

Pathogen
Herpes simplex virus-1 (HSV-1)
Herpes Simplex virus-2 (HSV-2)
Varicella zoster virus (VZV)
Epstein-Barr virus (EBV)
Cytomegalovirus (CBV)
Human herpesvirus-6 (HHV-6)
Human herpesvirus-7 (HHV-7)
Karposi sarcoma-associated herpesvirus (KSHV/HHV-8)
Hepatitis B virus (HBV)
Hepatitis C virus (HCV)

Pathogen
Human immunodeficiency virus (HIV)
Human T-cell lymphotropic virus (HTLV-1)
Human papillomavirus (HPV)
Polyomavirus JC/BK
Merkel cell polyomavirus
Borrelia burgdorferi
Chlamydia trachomatis
Helicobacter pylori
Staphylococcus aureus
Toxoplasma gondii

Proposed Associations with Inflammatory Disease

Pathogen
Herpes simplex virus-1 (HSV-1)
Herpes Simplex virus-2 (HSV-2)
Varicella zoster virus (VZV)
Epstein-Barr virus (EBV)
Cytomegalovirus (CBV)
Human herpesvirus-6 (HHV-6)
Human herpesvirus-7 (HHV-7)
Karposi sarcoma-associated herpesvirus (KSHV/HHV-8)
Hepatitis B virus (HBV)
Hepatitis C virus (HCV)

Pathogen
Human immunodeficiency virus (HIV)
Human T-cell lymphotropic virus (HTLV-1)
Human papillomavirus (HPV)
Polyomavirus JC/BK
Merkel cell polyomavirus
Borrelia burgdorferi
Chlamydia trachomatis
Helicobacter pylori
Staphylococcus aureus
Toxoplasma gondii

Methodological approach

- Multiplex immunoassay – Luminex
  1. Sensitive
  2. Semi-quantitative
  3. Up to 90 antigens in single reaction
- Proposed collaboration with Dr Michael Pawlita in Heidelberg
  1. > 80 % proposed antigens have assays on Luminex
  2. Already has access to reference sera and validation against existing “Gold Standard” assays of antibody quantitation
  3. Plan to collaborate with other ‘experts’ for each pathogen

Proposed Methodological Stages

1. Development and validation of outstanding antibody assays on Luminex
2. Transfer of technology to UKB laboratories
3. Sequential multiplex reactions combining different antibodies until approximate '50-plex' achieved
   - ensuring consistent assay performance
4. Pilot study with 5000 samples performed simultaneously in Heidelberg and UKB
5. First phase of 20,000 samples (10,000 baseline and 10,000 follow-up)
6. Final phase to complete assessment of 600,000 (500,000 baseline and 100,000 follow-up)

Quality Assurance and Timelines

- Involvement of independent ‘experts’ for each pathogen
- Development of internal quality control schedule
- Sample selection strategy to minimise systematic bias related to participant phenotypes / collection strategy

- Expect assay development to take 24 months
- Expect assays to take further 18 – 24 months
- Expected Total 5 year project duration

Beneficial Outcomes

- Depth and breadth of data consistent with other UK Biobank data
- Cost-effective
- Logistically feasible
- Scientifically robust
- Valuable resource for spectrum of scientific and public health disciplines

Contact

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