University of Glasgow

Viruses and childhood leukaemia

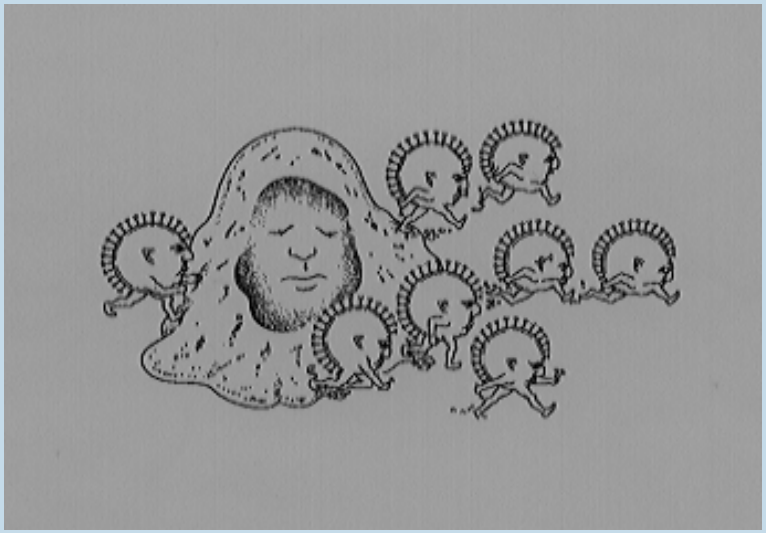
Ruth Jarrett

Viruses and childhood leukaemia

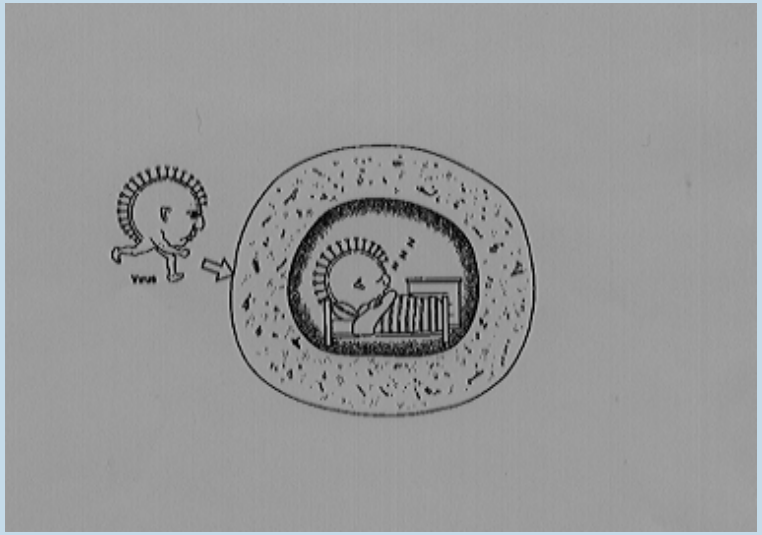
- **Direct role**
  - **Some or all of the virus genome is present in all the tumour cells**
- **Indirect role**
  - **Viral sequences may not be present in tumour cells**
  - **Host may have cleared viral infection**

Viral infection may be latent or lytic

Lytic infection



Latent infection



Viral expression is usually tightly restricted in tumour cells

Exclusion of known viruses as direct agents

Herpesviruses

- VZV
- HCMV
- EBV
- HHV-6
- HHV-7
- HHV-8

Polyomaviruses

- JC virus
- BK virus
- Merkel cell virus
- SV40

Screening for known viruses

Retroviruses

- HTLV-1

egenerate PCR assays

- Degenerate PCR assays are used to detect novel viruses related to known viruses, i.e., new members of a virus family
- Degenerate PCR assays for herpesviruses have failed to find new members of this virus family in common ALL
- Degenerate PCR assays for polyomaviruses have similarly failed to detect novel viruses, but these assays are less robust than the herpesvirus assays

Representational difference analysis

- **Technique to identify differences between two complex genomes**
- **Can be used to detect exogenous DNA, i.e., viral genomes**
- **No *a priori* knowledge of virus required**
- **Proven track record – HHV-8**
- **Works best for viruses with large genomes and where viral genome present at least at single copy level**
- **Only part of cellular genome (representation) used in each experiment**
- **More representations leads to greater chance of finding virus**
- **We analysed 20 representations (5 x 4 independent representations) from 11 cALL patients**
- **No exogenous sequences detected**

Is a virus directly involved in childhood leukaemia?

Has direct involvement of a viral agent been excluded

No

Small genomes or remnants of larger genomes could have been missed

The future

Second generation sequencing of complete transcriptomes from leukaemic cells followed by digital subtraction

‘Third generation’ sequencing of complete genomes of leukaemic cells coupled with digital subtraction