



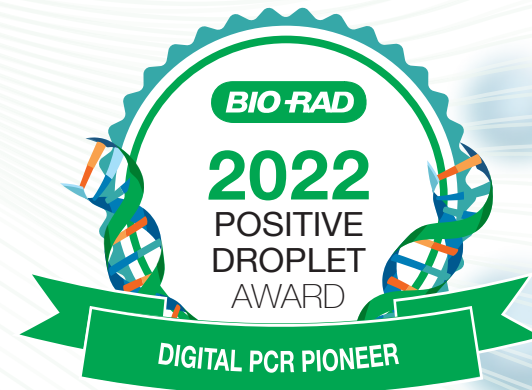
## Alec Morley, MD

**Emeritus Professor**

**Department of Haematology and Genetic Pathology**

**Flinders University (Australia)**

**Category: Digital PCR Pioneer**



## Impact of Droplet Digital PCR on Dr. Alec Morley's Research

In the late 1980s, my laboratory developed the methodology to sequence the rearranged immunoglobulin and T cell receptor genes with the aim of using the clonal rearrangements present in leukaemia as a molecular marker for the disease. At the time, we were quantifying somatic mutations in human lymphocytes using high efficiency cloning in tissue culture and quantitation using Poisson statistics. We translated this cellular approach to the molecular level, combined allele-specific oligonucleotide PCR (ASO-PCR) with the quantitative approach and developed limiting dilution PCR (LD-PCR), which we then proposed as a general method for quantifying PCR targets. Some years later LD-PCR was renamed digital PCR. Our first use of LD-PCR was to show that in childhood acute lymphoblastic leukaemia (ALL) the level of residual disease at the end of induction predicted clinical outcome. Other groups subsequently confirmed this finding and adjusting treatment according to the level of residual disease has become part of standard management in ALL and other haematological disorders. During the 1990s, we used limiting dilution PCR for numerous studies of biological and clinical features in leukaemia and myeloma in marrow and blood.

At the time, the technique was laborious as it involved performing numerous PCR reactions and using gel electrophoresis to confirm the all-or-none endpoint of each. We therefore switched to using real-time qPCR soon after it had been described. It was only after passage of some years that the development of new instrumentation enabled digital PCR to become a technique able to be used widely. Our current studies are directed to very sensitive detection of residual disease, and this requires amplification of large masses of DNA. We therefore continue to use real-time qPCR for most of our studies but routinely use Droplet Digital PCR for measurement of copy number.

## About Dr. Alec Morley

Alec Morley's career involved clinical and laboratory haematology, teaching, and research. Research areas included periodic diseases, aplastic anaemia, human somatic mutation, biology of ageing and genetic toxicology. His laboratory pioneered study of minimal residual disease in hematologic cancer and developed and applied molecular techniques for diagnosis and monitoring of disease. Such techniques include the original descriptions of digital (limiting dilution) PCR and its use for quantifying residual disease in leukemia, detection of lymphocyte clonality by PCR, detection of the *BCR-ABL* transcript by PCR, and High-Annealing-Temperature (HAT) PCR.

## Dr. Alec Morley's Key Publications

- [Quantitation of targets for the polymerase chain reaction by use of limiting dilution](#)
- [Outcome prediction in childhood acute lymphoblastic leukaemia by molecular quantification of residual disease at the end of induction](#)
- [Digital PCR: A brief history \*Biomolecular Detection and Quantification\*](#)