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Method for single nucleotide resolution mapping of abasic (AP) sites

Professor Sir Shankar Balasubramanian & his team have developed a novel method for single nucleotide resolution mapping of AP sites (including endogenous sites) in genomic DNA.

Applications:

- Identification of AP sites as biomarker in liquid/solid biopsies as prognostic/diagnostic for cancer
- Adaptation of method to map any modified or mismatched base for which a glycosylase is available, by artificial generation of AP sites *via* glycosylase activity and subsequent mapping

Benefits of the Method:

- Works effectively & selectively on synthetic DNA models
- Can map abnormal base sites, such as 5-hmU and 8-oxoG by additional enzyme step
- Using equal input amounts of synthetic DNA containing AP, 5-fU, 5-fC or GCAT bases, over 93% of total sequencing reads align to AP-DNA
- Selectivity is over 200-fold relative to 5-fU and over 2000-fold relative to 5-fC

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Background

The ability to accurately detect the presence and location of abasic (AP) sites in genomic DNA is challenging; PCR amplification & sequencing is not possible since many polymerases are unable to read through AP sites

Technology

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Key Features

- Uses a novel probe that reacts cleanly with AP sites to pull down AP containing regions
- Ensures selectivity for AP sites
- Allows single nucleotide resolution mapping of captured sites
- In glycosylase mode, it provides finer mapping of abnormal nucleotide sites compared to previously developed methods

Applications

- Since AP levels are elevated in cancer, identification of AP sites serves as a biomarker in liquid/solid biopsies as prognostic/diagnostic for cancer
- The method may be adapted to map any modified or mismatched nucleotide for which a glycosylase is available, by artificial generation of AP sites via glycosylase activity and subsequent mapping:
    - demonstrated in model synthetic DNA using SMUG1 glycosylase to map T-modifications
    - SMUG1-AP mapping in *Leishmania major* genomic DNA identifies 5-hydroxymethyluracil sites at single nucleotide resolution
- Selectivity is over 200-fold relative to 5-fU and over 2000-fold relative to 5-fC

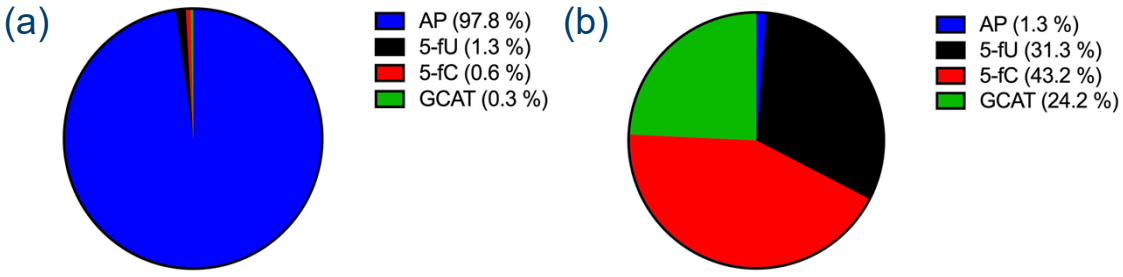

Figure 1. Comparison of (a) the new method, with (b) standard Illumina library preparation and direct sequencing. Graphs show relative proportion of post-sequencing reads aligned to each model DNA containing a single DNA modification. Whilst abasic sites are underrepresented using current library preparation methods, the new method successfully enriches for abasic sites

Commercialisation

We are seeking a commercial partner for collaboration and/or licensing of this technology, which is protected by patent application no. GB1812283.8 filed on 27th July 2018