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Soutenance de thèse

G4-Hunter: Un nouvel algorithme pour la prediction des G-quadruplexes.

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Biologically relevant G4 DNA structures are formed throughout the genome includ- ing immunoglobulin switch regions, promoter sequences, minisatellites and telomeric repeats. They can arise anywhere in the genome or transcriptome where single-stranded G-rich DNA or RNA sequences are exposed during replication, transcription or recombination.
Computational analysis using predictive algorithms suggests that the human genome contains approximately 370,000 potential G4-forming sequences [1,2]. These predictions are generally limited to the standard G3+N(1-7)G3+N(1-7)G3+N(1-7)G3+ description (four runs of 3 or more Gs separated by loop of 1-7 nucleotides). However, many stable G4s defy the standard description and escape this consensus; this is the reason why broadening this description should allow the prediction of more G4 loci.
We propose an objective score function, G4-hunter, which predicts G4 folding propensity from a linear nucleic acid sequence. The new method focus on guanines clusters and GC asymmetry, taking into account the whole genomic region rather than individual quadruplexes sequences. In parallel with this computational technique, a large scale in vitro experimental work has also been developed to validate the performance of our algorithm in silico on hundreds of different sequences. G4-hunter exhibits unprecedented accuracy and sensitivity and leads us to reevalu- ate significantly the number of G4-prone sequences in the human genome [3]. G4-hunter also allowed us to predict potential G4 sequences in HIV [4] and Dictyostelium discoideum [5], which could not be identified by previous computational methods.

Mots clés: Algorithm, G-quadruplex, DNA, Dictyostelium

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