INTELLIGENT ACQUISITION AND AUTOMATED ANALYSIS OF RANDOM CELL MIGRATION IN HIGH-CONTENT SCREENING

de Bont H, Rogkoti MV, van de Water B and Le Dévédec SE
Toxicology Department, Leiden Academic Center for Drug Research, Leiden University, The Netherlands
E-mail: s.e.ledevedec@lacdr.leidenuniv.nl

Abstract
In this study, we describe a fully automated high-content time-lapse fluorescence microscopy system including image acquisition and analysis that allows the tracking of fast moving cancer cells. High-content screening using image-based assays is becoming increasingly important. Fluorescence microscopy is a powerful tool to study complex biological processes with high spatiotemporal resolution. Analysis of the tumour cell migratory behaviour in vitro in response to compounds or genetic manipulations is routinely used to unravel the mechanisms of increased invasion capacity in metastatic cancer. In high-content screening, quantitative microscopy depends highly on imaging a large number of cells. On the other hand, cell migratory behaviour is largely dependent on the cell density. Manual selection of specific field of views with a similar and appropriate cell number is unfortunately time-consuming in high-content screening. We designed a macro that guides the microscope to automatically detect imaging fields with a number of cells chosen by the experimentalist. We tested the relevance of this intelligent image acquisition in a random cell migration assay using three aggressive breast cancer cell-lines at different densities. As a result, we demonstrate that there is a clear correlation between cell density and tumour cell migratory behaviour (e.g. speed and persistence). In addition, by using this macro we significantly decrease the variation in imaged number of cells per field of view and consequently reduced the standard deviation in measured motility parameters. In conclusion intelligent automated image acquisition is highly relevant for studying cell migratory behaviour in a high-content screening approach.