Motion vector analysis of the line-patterned cardiomyocytes for assessing the toxicity of anticancer drugs on left ventricular function

Atsuhiko Naito, Masamichi Ito, Hiroko Izumi-Nakaseko, Fengying Gao, Akihiro Furuya, Mihoko Hagiwara-Nagaswa, Ryuichi Kambayashi, Koki Chiba, Ai Goto, Atsushi Sugiyama


Recent findings highlight the unexpected toxicity of anticancer drugs on left ventricular (LV) function. Nevertheless, a strategy to predict the potential toxicity of drugs on LV function is still limited. In the present study, we developed a novel culture system with patterned human induced pluripotent stem cell-derived cardiomyocytes (hiPSCMs) in a 96 well format and evaluated the acute-to-chronic effects of several anticancer drugs by our system. We found that doxorubicin exhibited chronic, not acute, robust toxicity on the movement of hiPSCMs. The toxicity of molecule-targeted anticancer drugs was generally mild, however, sunitinib impaired the contraction, relaxation and synchronicity of contraction more strongly than other molecule-targeted anticancer drugs. We also identified that synchronicity of contraction was impaired only by the anticancer drugs with warning on LV toxicity. Patterned hiPSCMs also exhibited distinct, mechanism of action-based, contractile responses against various cardioactive compounds. These results collectively suggest the usefulness of patterned hiPSCMs in assessing the effect of drugs on LV function.