

P013 Reorganisation of the endocytic pathways of multidrug resistant cells

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A current problem with a number of conventional chemotherapy regimes is the capacity of cells to desensitise themselves to a range of drugs and become multidrug resistant (MDR). Thus novel systems are urgently required to target these cells and overcome the resistance phenotype. However, the design of effective macromolecular therapeutics, that requires internalisation to mediate their effects, requires a high level of understanding of the endocytic pathways of these MDR cells. We show comparative data from phenotypic profiling studies of the endocytic pathways of parental and doxorubicin resistant HL60 acute myeloid leukaemia cells. We find that distribution of both early and late components of the endocytic pathways is modified in the resistant cells and that this mirrors the distribution of daunorubicin. These resistant cells are thought to have a higher capacity to sequester weak-base drugs such as doxorubicin and daunorubicin in endocytic vesicles but contrary to previous reports, we find that both parental and resistant cells have equal capacity to acidify their endocytic pathways. This suggests that acid-sequestration is not a major contributor to the resistant phenotype but demonstrates any changes in endocytic features of resistant cell could influence the intracellular dynamics and efficacy of therapeutic entities.