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**TARGETING PROLIFERATING CHRONIC LYMPHOCYTIC LEUKAEMIA CELLS WITH A NOVEL SYNTHETIC LOW DENSITY LIPOPROTEIN DRUG DELIVERY SYSTEM**

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**Background.** Chronic lymphocytic leukaemia (CLL) currently remains incurable without stem cell transplantation, an option for only the minority of patients. Despite advances in chemotherapy, most patients relapse owing to the persistence of minimal residual disease (MRD). Substantial evidence has accrued to suggest that the tumour microenvironment is central to disease progression in CLL, with the bone marrow (BM) and lymph nodes (LN) acting as sanctuary sites for MRD. Whilst peripheral blood CLL cells are cell cycle arrested, significant rates of clonal proliferation occur in the BM/LN wherein acquisition of deleterious cytogenetic abnormalities such as 17p deletion may arise. Further, CLL cells co-cultured *in vitro* on stroma with CD154/IL-4 to give a proliferative signal, are chemoresistant to first line therapies. As proliferating cells require lipids for membrane synthesis, we hypothesise that proliferating CLL cells will have greater requirement for low density lipoprotein (LDL) compared to circulating CLL cells, and also that of normal resting lymphocytes providing a potentially differential cellular property to attack. Proof of concept of drug-loaded synthetic (s)LDL nanoparticles has been provided in glioblastoma and CML. We propose that drug loading into sLDL nanoparticles will allow selective targeting of proliferating CLL cells within the BM/LN proliferation centre, will protect drugs from plasma binding proteins, and will ultimately raise intracellular drug concentrations in the protective microenvironmental niche, to overcome chemoresistance. **Aims.** To determine (a) the extent of sLDL uptake by CLL cells compared to normal; and (b) whether sLDL uptake by CLL cells changes under proliferative conditions mimicking the proliferation centre. This will determine whether proliferating CLL cells have increased sLDL uptake compared to non-cycling CLL cells or normal B lymphocytes. **Methods.** sLDL uptake was assessed by flow cytometry, measuring the mean fluorescence intensity in the FITC channel owing to the stable incorporation of dioctadecyloxycarbocyanine (DiO) into the formulation. Internalisation was confirmed by deconvolution fluorescence microscopy. Primary CLL and normal donor samples were enriched for CD19+ B-lineage cells by magnetically activated cell sorting. Cells were cultured in media on tissue culture plastic or NT-L mouse fibroblasts with or without CD154/IL4. Lymphoid cells were stained with CellTrace VioletR to track cell division in response to proliferative signals (CD154/IL4 stroma). **Results.** HG3, a human lymphoblastoid cell line, avidly took up sLDL nanoparticles in a concentration (0-50 ng/mL cholesterol) and time (0.5-24h) dependent manner. Normal donor peripheral blood B-cells and CLL cells cultured on plastic did not actively take up sLDL but maintained their viability even in the highest concentration sLDL tested. Actively proliferating CLL cells on CD154/IL4 stroma could be targeted with sLDL unlike their non-cycling counterparts; interestingly even the minor population of cells that had remained undivided on stroma were also found to be sLDL positive. **Summary.** CLL cells can be selectively targeted by sLDL nanoparticles with respect to their non-cycling counterparts. We next will investigate the *in vivo* targeting of sLDL which we hypothesise, by virtue of their size, will home to lymphoreticular organs, sanctuary sites for CLL MRD.