Development of Human Multiple Myeloma in NOD/SCID Mice with Multiple Bone Involvement

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Multiple myeloma (MM) is characterised by the accumulation of neoplastic plasma cells in multiple sites throughout the bone marrow (BM). It would be invaluable to study human MM in a physiologically appropriate humanised animal model, in which transplanted human MM cells home to and repopulate multiple bone sites.

In this study, we used a novel conditioning regimen to prepare nonobese diabetic severe combined immunodeficiency (NOD/SCID) mouse recipients before transplantation of human MM RPMI8226 cells. Following RPMI8226 transplantation, human (hu) CD38+ MM cells were detected in the BM of all preconditioned recipients (n=19, mean: 3% total BM cells), compared to only 19% of non-conditioned recipients (n=16, mean: 0.85% total BM cells). MM infiltration of multiple bone sites was observed in all preconditioned recipients, 65% of which exhibited infiltration of all bone sites tested (femurs, hips, humeri, spine, skull). Only 44% of the non-conditioned recipients exhibited infiltration of bone sites, and the majority of these involved only a single site. Serum paraprotein (I light chain immunoglobulin) was detected 4 weeks post-transplant, at a >500-fold higher concentration in preconditioned, compared to non-conditioned recipients (mean concentration= 561 m g/ml ± 105ug/ml vs 1.4 m g/ml ± 0.7ug/ml respectively). Similar levels of paraprotein could not be detected in non-conditioned recipients until 4 weeks later, (8 weeks post-transplant). Hind-limb paralysis was also observed in 79% of the preconditioned recipients vs 18% of the non-conditioned recipients. All of the preconditioned recipients developed MM disease and required sacrificing before 11 weeks post-transplant, whereas only 60% of non-conditioned recipients required sacrifice before 14 weeks post-transplant (end-point of experiment). Thus, our model allows MM cell infiltration at multiple BM sites, typical of human MM and as such, represents a significant improvement on current experimental models. This new humanised model will facilitate studies on MM pathology and enable preclinical testing of novel anti-MM therapies.