Response to "CD20 positive cells are undetectable in the majority of multiple myeloma cell lines and are not associated with a cancer stem cell phenotype". Haematologica 2012;97(7):1110-4

It is with interest that I read the article by Paino *et al.*[1] addressing the absence of CD20$^+$ cells in the majority of multiple myeloma cell lines and that CD20$^+$ is not associated with the stem cell phenotype. The research was carried out with commercially available multiple myeloma cell lines. The article reports that the author did not find expression of CD20$^+$ on examined cell lines. The paper suggests that myeloma cancer stem cells may not express CD20$^+$.

Matsui *et al.*[2] characterized clonogenic multiple myeloma cells and found CD138$^+$ and CD138$^-$ cells. CD138$^-$ cells were considered post germinal center cells, the proliferation of which could be inhibited by the anti-CD20$^+$ antibody. CD138$^+$ cells were considered more mature and did not express CD20$^+$.

The reports are contradictory in so far that post germinal center cells express CD20$^+$[2] whereas cells that should be more immature, named myeloma stem cells, do not express CD20$^+$.[1] This would suggest that myeloma stem cells upon maturation to post germinal center B cells start to express CD20$^+$. The question is whether commercially available cell lines represent multiple myeloma stem cells *in vivo*.

Plasma cells normally reside in the spleen and lymph nodes, and can also be found in the thymus. They generally do not circulate in the peripheral blood, unless after stimulation.[3] In normal circumstances, they make up less than 1% of bone marrow cells.[4] Plasma cells are mature B cells that may have their origin in lymphoid tissues and home among others in the bone marrow. Expression of CD20 has been reported in pre-B cells, mature B cells and on plasma cells.[5]

The author[1] refers to publications of anti-CD20 therapy post autologous transplants, one in which CD20 expression was not determined, and claims that anti-CD20 therapy cannot eradicate multiple myeloma stem cells.

Ohno reported complete remission in a 72-year old stage III CD20$^+$ multiple myeloma patient, treated by one course of melphalan, predinison and rituximab with rituximab maintenance.

It is likely that myeloma develops out of plasma cells in the bone marrow, and not out of cells in the lymphoid tissue; therefore, not all cells may express anti-CD20.

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