CDB SEMINAR

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Thursday, August 1, 2013
14:00~15:00 A7F Seminar Room

B cell progenitors and precursors change their microenvironment in fetal liver during early development

Summary

The microenvironments, in which B-lymphocytes develop in fetal liver, are largely still unknown. Among the non-hematopoietic cells we have identified and FACS-separated two subpopulations, $CD45^{-}TER119^{-}VCAM\text{-}1^{+}$ cells that are either $CD105^{high}LYVE\text{-}1^{high}$ or $CD105^{low}ALCAM^{high}$. Immunohistochemical analyses find three of four $c\text{-}Kit^{+}IL\text{-}7R\alpha^{+}B220^{low}CD19^{-}SLC^{-}$ B-progenitors in contact with vascular endothelial-type $LYVE\text{-}1^{high}$ cells on embryonic day 13.5. One day later $c\text{-}Kit^{+}IL\text{-}7R\square^{+}$ cells develop to $CD19^{- \text{ and } +}$, SLC-expressing, DHJH-rearranged pre/pro and pro/preB-I cells. Less than 10% are still in contact with $LYVE\text{-}1^{high}$ cells, but half of them are now in contact with mesenchymally-derived $ALCAM^{high}$ liver cells. All of these $ALCAM^{high}$ cells, but not the $LYVE\text{-}1^{high}$ cells produce IL-7 and CXCL12, while both produce CXCL10. Progenitors and pro/preB-I cells are chemo-attracted *in vitro* towards CXCL10 and 12, suggesting that lymphoid progenitors with Ig gene loci in germline configuration enter the developing fetal liver at E13.5 from vascular endothelium, attracted by CXCL10, and then migrate within a day to an $ALCAM^{high}$ liver cell-microenvironment, differentiating to DHJH-rearranging, surrogate light chain-expressing pre/proB and pro/preB-I cells, attracted by CXCL10 and 12. Between E15.5 and E16.5 preB-I cells expand 10 fold in continued contact with $ALCAM^{high}$ cells, and begin VH- to DHJH-rearrangements in further differentiated $c\text{-}Kit^{-}IL\text{-}7R\alpha^{-}$ preBII cells.

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