Supplementary Figure Legends

Supplementary Figure 1. The Ras-MEK signaling pathway regulates cyclin expression. *Irf4*$^{-/-}$*Irf8*$^{-/-}$ pre-B cells expressing MIGR1, DN-Ras or DN-MEK were cultured in medium with or without IL-7 for 24 hours. (**a**) qPCR for *Ccnd2* expression; †P<0.001 as compared with mock infected +IL-7 *Ccnd2* expression. (**b**) qPCR analysis for *Ccne* expression; †P<0.001 as compared with mock infected +IL-7 *Ccne* expression and *P<0.001 as compared with –IL-7 *Ccne* expression. (**c**) Immunoblot for cyclin D2 and cyclin E from *Irf4*$^{-/-}$*Irf8*$^{-/-}$ pre-B total cell lysates. Cells were cultured according to the conditions described above. Actin immunoblot serves as an internal loading control. Data are representative of three independent experiments with differences between cyclin D3 protein with or without either inhibitor being significant (P<0.001). (**d-e**) qPCR analysis for (**d**) *p21Cip1* expression and (**e**) *p27Kip1* expression; *P<0.001 as compared with mock infected -IL-7 *p27Kip1* expression. *B2m* was used as the endogenous reference gene. Data represent mean ± SD from four independent experiments.

Supplementary Figure 2. Aiolos suppresses *Ccnd2* and *Ccne* but has no effect on expression of *Rag* or *Igκ* germline. *Irf4*$^{-/-}$*Irf8*$^{-/-}$ pre-B cells expressing either MIGR1 alone or Aiolos were cultured in medium with or without IL-7 for (a-b) 24 or (c-d) 48 hours. (**a**) qPCR for *Ccnd2* and *Ccne* expression; †P<0.001 as compared with mock infected +IL-7 *Ccnd2* expression; $^{\$}$P<0.01 as compared with mock infected –IL7 *Ccnd2* expression; *P<0.001 as compared with mock infected +IL-7 *Ccne* expression; $^{\#}$P<0.001 as compared with mock infected –IL-7 *Ccne* expression. (**b-d**) qPCR for (**b**) *p21Cip1* and *p27Kip1* expression, (**c**) *Rag1* and *Rag2* expression and (**d**) *Igκ* germline transcription.

For all quantitative real time PCR analysis *B2m* was used as the endogenous reference gene. Data represent mean ± SD from four independent experiments.

Supplementary Figure 3. Ras signaling does not suppress *Ccnd2* and *Ccne* transcription in *Aiolos*$^{-/-}$ B cell progenitors. (**a-b**) Pre-B cells ($CD19^{+}CD43^{low}IgM^{-}$) were sorted from WT or *Aiolos*$^{-/-}$ bone marrow. Cells expressing either mock MIGR1 or CA-Ras were cultured in the presence of IL-7 (7.5ng/ml) for 48 hours. qPCR analysis for (a) *Ccnd2* and (b) *Ccne* in WT and *Aiolos*$^{-/-}$ pre-B cells; $^{\dagger}P<0.001$ as compared with *Ccnd2* expression in mock infected WT and *P<0.001 as compared with *Ccne* expression in mock infected WT. *B2m* was used as the endogenous reference gene.

Supplementary Figure 4. Specificity of the Ras-MEK-Id3 signaling pathway. (**a-b**) *Irf4*$^{-/-}$*Irf8*$^{-/-}$ pre-B cells expressing MIGR1 alone, DN-Ras or DN-MEK were cultured in medium with or without IL-7 for 24 hours. qPCR analysis for (a) *Id1* and (b) *Id2* expression; $^{\dagger}P<0.001$ as compared with mock infected +IL-7 *Id2* expression and *P<0.001 as compared with –IL-7 *Id2* expression. *B2m* was used as the endogenous reference gene. Data represent mean ± SD from four independent experiments. (**c-d**) qPCR analysis for (**c**) *Ccnd3*, *Ccnd2* and *Ccne* and (**d**) *p21Cip1* and *p27Kip1* expression in *Irf4*$^{-/-}$*Irf8*$^{-/-}$ pre-B cells expressing ER-Id3 cultured in medium with or without IL-7 for 24 hours. Cells were either mock treated with ethanol (solvent of 4-OH-tamoxifen) or 4-OH-tamoxifen (1μM) to induce *Id3* expression. *B2m* was used as the endogenous reference gene. Data represent mean ± SD from four independent experiments.

Supplementary Figure 5. IL-7 does not modulate *in vitro* E2A binding activity. *In vitro* binding of E47 was assayed by EMSA. Nuclear extracts were prepared from *Irf4*$^{-/-}$ *Irf8*$^{-/-}$ pre-B cells cultured in medium with or without IL-7 for 30 hours and cells were treated with MEK inhibitor (MEK-i, 10μM of PD 98059) for the last six hours of culture. An equal amount of nuclear protein was used for each reaction. E2A binding was assayed using the κ*E1* probe. E47/DNA complexes were verified using an E47 antibody.

Supplementary Figure 6. Id3 does not regulate cyclin expression. CD19^{+} cells were isolated from bone marrow of WT or *Id3*$^{-/-}$ mice and were cultured in the presence of 10ng/ml IL-7 for 48 hours and then cultured for another 24 hours in medium with or without IL-7. qPCR analysis for *Ccnd3*, *Ccnd2* and *Ccne* expression. *B2m* was used as the endogenous reference gene. Data represent mean ± SD from three independent experiments.

Supplementary Figure 7. Model of how signals through the IL-7R and pre-BCR coordinate proliferation and *Igκ* recombination. Our data demonstrate that pre-BCR mediated Ras/MEK/ERK activation inhibit proliferation and induce *Igκ* recombination through mutually exclusive mechanisms. ERK activation inhibits proliferation by inducing Aiolos which attenuates *Ccnd3* transcription. In contrast, ERK activation augments *Igκ* germline transcription by inducing E2A and suppressing Id3 thereby increasing the amount of free E2A available for binding to the *Igκ* enhancers. The downstream activities of both Aiolos and E2A are antagonized by IL-7R mediated STAT 5 activation. STAT 5 represses Aiolos-mediated silencing of *Ccnd3* while it suppresses

Igκ transcription by directly binding to $E_{\kappa i}$ and preventing E2A recruitment. In this model, the relative binding of STAT 5 and E2A to the $E_{\kappa i}$. determine *Igκ* germline transcriptional activity. Signaling through the pre-BCR also induces IRF-4 and IRF-8 which enhance *Igκ* transcription through the $E_{\kappa 3'}$[22]. Additionally, IRF-4 and IRF-8 may indirectly promote *Igκ* recombination by facilitating the migration of pre-B cells into IL-7 deficient bone marrow niches and by cooperating with Ras to induce Aiolos and silence *Ccnd3*[20,22].

Supplementary Table 1

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Quantitative PCR	
Cyclin D3-Fw	5'-CGC TGC GAG GAG GAT GTC TT-3'
Cyclin D3-Rev	5'-CAA CTG CCA TGG AGC CAC AG-3'
Cyclin D2-Fw	5'-AGC TGT CCC TGA TCC GCA AG-3'
Cyclin D2-Rev	5'-GCA GCT CTG TCA GGG CAT CA-3'
Cyclin E-Fw	5'-CCC CAG GAC TGC ATT TCA GC-3'
Cyclin E-Rev	5'-TGA CGC TGC AGA AAG TGC TCA-3'
p21-Fw	5'- GTG AGC AGT TGC GCC GTG AT-3'
p21-Rev	5'-GGG AAT CTT CAG GCC GCT CA-3'
p27-Fw	5'-GGC AGC TTG CCC GAG TTC TA-3'
p27-Rev	5'-TCG CTT CCT CAT CCC TGG AC-3'
B-2Microglobulin-1	5'-AGA CTG ATA CAT ACG CCT GCA-3'
B-2Microglobulin-2	5'-GCA GGT TCA AAT GAA TCT TCA-3'
Q-Rag1L	5'-CTG CAG ACA TTC TAG CAC TC-3'
Q-Rag1R	5'-AAC TGA AGC TCA GGG TAG AC-3'
Q-Rag2L	5'- TCA TAA GTG AGA AGC CTG GT-3'
Q-Rag2R	5'-CCT TCA GTG CCA AAA TAA GA-3'
k-GL-Fw	5'-GAG GGG GTT AAG CTT TCG CCT ACC CAC-3'
k-GL-Rev	5'-GTT ATG TCG TTC ATA CTC GTC CTT GGT CAA-3'
Aiolos-Fw	5'-GAC ACG TGC CCT ATG ACA ACA GCA G-3'
Aiolos-Rev	5'-GCA TGC GTA GTT GCA GAG GTG ACA C-3'
Ikaros-Fw	5'-AAG TCT GTG TCA TCG GAG CGA GAG G-3'
Ikaros-Rev	5'-CAT CCT GCG AGT TCT CTG AGG C-3'
IL-7 receptor-Fw	5'-GCC CAG CAA GGG GTG AAA GCA AC-3'
IL-7 receptor-Rev	5'-GGC AAG ACA GGA TCC CAT CCT CC-3'
Id1-Fw	5'-TTC AGC CTC CAG AGA CTT TGG G-3'
Id1-Rev	5'-CCG AGA AGC ACG AAA TGT GAC-3'
Id2-Fw	5'-CCT GAA CAC GGA CAT CAG C'-3'
Id2-Rev	5'-CAC AGA GTA CTT TGC TAT CAT TCG-3'
Id3-Fw	5'-CAC TTA CCC TGA ACT CAA CGC C-3'
Id3-Rev	5'-CCC ATT CTC GGA AAA GCC AG-3'
Kappa Recombination	
degVk	5'-GGC TGC AGS TTC AGT GGC AGT GGR TCW GGR AC-3'
MAR (Igκ intron)	5'-AAC ACT GGA TAA AGC AGT TTA TGC CCT TTC-3'
k-meth-F	5'-ATG ACC CAG AGG ATG AAA C-3'

EMSA: Biotinylated at 5' end and non-biotinylated	
κ-Ebox1-Fw	5'-TCC GAG AGG CCA TCT GGC AGT TGC TTA AG-3'
κ-Ebox1-Rev	5'-CTT AAG CAA CTG CCA GAT GGC CTC TCG GA-3'
κ-Ebox1-Mut-Fw	5'-TCC GAG AGG CGT AGT GGC AGT TGC TTA AG-3'
κ-Ebox1-Mut-Rev	5'-CTT AAG CAA CTG CCA CTA CGC CTC TCG GA-3'
FcγR1-Fw	5'-ATG TAT TTC CCA GAA AAG G-3'
FcγR1-Rev	5'-CCT TTT CTG GGA AAT ACA T-3'
ChIP	
Igk-kEi (Stat5 ChIP) Fw	5'- TTTGAC CCTTCCCTGCCAAA-3'
Igk-kEi (Stat5 ChIP) Rev	5'-CAACTGTAATCTGGG CCACCTG-3'
Cish Fw	5'-CAGCGATACGATTGGTCAACTCT-3'
Cish Rev	5'-TGCGAACAGCTTGGAAGGAC-3'
Rnu7 (U7) up	5'-CTTCGGCTTTAGCTCCAAG-3'
Rnu7 (U7) down	5'-GCGGAAGTGCGTCTGTAG -3'
α-Amylase up	5'-CAGCTGTGCACATCATTG-3'
α-Amylase down	5'-TTCCTTGGCAATATCAACC-3'
Igk-kEi (E2A ChIP) Fw	5'-GGGGGAAAGGCTGCTCATAA-3'
Igk-kEi (E2A ChIP) Rev	5'-GCCACACCAGAACAGGTCAACT-3'