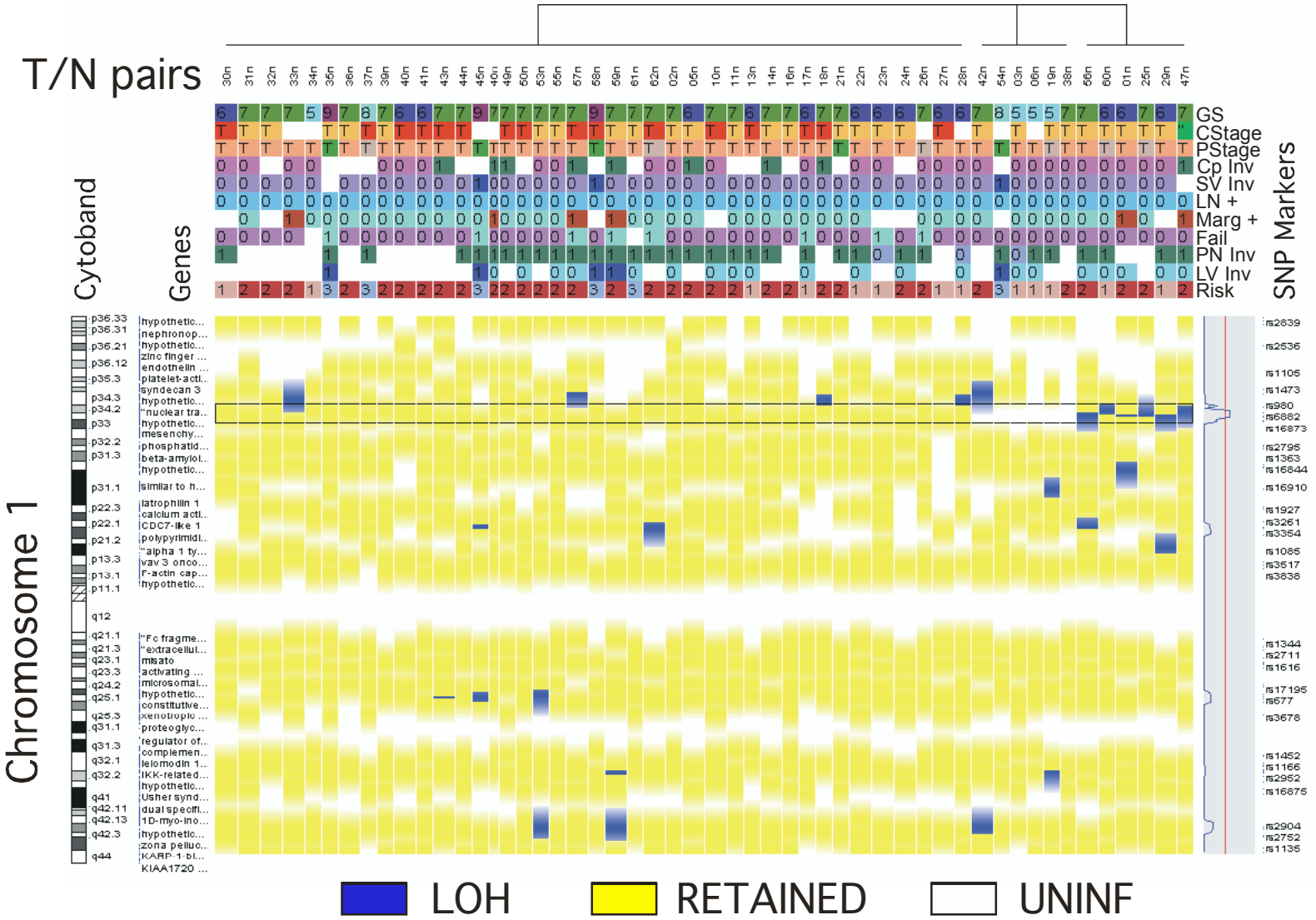Supplemental Figure 1A