The mouse has evolved to be the primary mammalian genetic model organism. Important applications include the modeling of human cancer and cloning experiments. In both settings, a detailed analysis of the mouse genome is essential. Multicolor karyotyping technologies have emerged to be invaluable tools for the identification of mouse chromosomes and for the deciphering of complex rearrangements. With the increasing use of these multicolor technologies resolution limits are critical. However, the traditionally used probe sets, which employ 5 different fluorochromes, have significant limitations. Here, we introduce an improved labeling strategy. Using 7 fluorochromes we increased the sensitivity for the detection of small interchromosomal rearrangements (700 kb or less) to virtually 100%. Our approach should be important to unravel small interchromosomal rearrangements in mouse models for DNA repair defects and chromosomal instability.