Why do my chimeras have red eyes and white fur?

The albino phenotype in mice (white hair and red eyes) arises from having homozygous mutant tyrosinase alleles (denoted as small "c"). Albino mice have melanocytes, but these cells are incapable of melanin synthesis. As tyrosinase heterozygous mice (Cc) produce sufficient tyrosinase (and are black with dark eyes), albino (c) is a recessive mutation, and albino mice are "cc". In contrast, black C57Bl/6 strain mice are CC.

The agouti (brown hair) phenotype comes in 17 variations, mostly due to the fact that the agouti locus is very complex. So while an agouti mouse phenotype varies from strain to strain, it is mostly brown or tan-yellow (aka "chinchilla"). The classic agouti brown phenotype seen in a 129-strain mouse is due to transposon-insertional mutagenesis of the alpha-MSH gene promoter in the agouti locus, which reduces the level of MSH peptide hormone in the mice. Since alpha-MSH activates eumelanin synthesis, a reduction in MSH results in more yellow phemelanin in the hair than black eumelanin, resulting in a yellow and black-banded mixture of fur (hence the "brown" agouti coat).

The agouti (A) allele is dominant to albino (c) and to non-agouti (a, or black) because the Aa heterozygous mice produce tyrosinase but cannot generate sufficient eumelanin. Therefore AA or Aa mice present as agouti, as long as they are also Cc or CC. And aaCc or aaCC mice are black because they make both tyrosinase and sufficient amounts of MSH and eumelanin.

Bottom line in terms of dominance: agouti (A) > black (a) > albino (c).

The UMMS TAMC uses C57BL/6J-Tyr[c-2J]/J (albino-B6) blastocysts or morulae for our ES cell injection experiments (unless otherwise specified by the client). This is because the C57BL/6-albino strain coat color alleles (aacc) are recessive to most other alleles found in commonly used strains of mouse ES cells.

Thus- if you are receiving chimeras from a 129 strain of ES cells- your chimeras will be brown (or yellow/tan for 129-Ola) on white. If you are receiving chimeras from a C57BL/6 strain of ES cells, your chimeras will be black on white (unless the strain of ES cells was from the C57BL/6 "restored agouti" Sanger JM8A3 ES cells- then it would be brown on white).