Origin and Fate of *de novo* Insertions of Transposable Elements in the Collaborative Cross

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Transposable elements (TEs) represent a large fraction of the mammalian genome and *de novo* insertions are known to contribute to disease causing mutations. By combining standard whole genome sequencing and a novel computational pipeline to the Collaborative Cross (CC) we have recently identified dozens of *de novo* TE insertions in this genetic reference population. The genomic context of these insertions is significantly different that the one observed for older TEs, strongly suggesting that many may have deleterious effects in gene function. If this hypothesis is correct, highly deleterious mutations should be purged from the corresponding CC strain while neutral mutations may rise in frequency and become fixed. Our extensive collection of CC samples from early generations to mice alive in the current colony provides an outstanding experimental setup to determine the origin and evolutionary trajectory of each mutation and determine whether there is evidence for selection. We selected four available CC strains with at least 9 *do novo* events (CC003/Unc, CC005/TauUnc, CC027/GeniUnc and CC055/TauUnc) and two CC strains that are not available from the UNC core (CC020/GeniUnc and CC074/Unc). We determined the origin and trajectory by genotyping a large cohort of mice of each strain with birthdates spanning from 2010 to 2018, including the most recent common ancestors of each strain. Our preliminary results indicate that *de novo* TEs originate at different generations within each pedigree and that, as predicted, there is a wide range of allele frequencies (5-100%). We will present detailed results for over 50 *de novo* TEs including some with strong deleterious effects.