



FIGURE 1. The SGA method for the construction of double mutant meiotic progeny and synthetic lethal analysis. First, a *MATα* strain carrying a query mutation (e.g., *bni1Δ*) linked to a dominant selectable marker, such as the nourseothricin-resistance marker *natMX*, which confers resistance to the antibiotic nourseothricin, and an *MFA1pr-HIS3* reporter, is crossed to an ordered array of *MAT a* viable yeast deletion mutants, each carrying a gene deletion mutation linked to a kanamycin-resistant marker (*kanMX*). Growth of resultant heterozygous diploids is selected for on medium containing nourseothricin and kanamycin. Second, the heterozygous diploids are transferred to medium with reduced levels of carbon and nitrogen to induce sporulation (which involves meiosis) and the formation of haploid meiotic spore progeny. Third, spores are transferred to synthetic medium lacking histidine, which allows for selective germination of *MAT a* meiotic progeny because only these cells express the *MFA1pr-HIS3* reporter specifically. Finally, the *MAT a* meiotic progeny are transferred to medium that contains both nourseothricin and kanamycin, which then selects for growth of double mutant meiotic progeny. Within budding yeast cells or spores, the gene deletions are represented as filled circles, whereas the wild-type gene is represented as an open circle. Double mutants that fail to grow are synthetically lethal (black arrow on lower right array). (Reprinted, with permission, from Tong et al. 2001 [©AAAS].)