Monarch research has also been at the forefront of integrating chemical ecology with genomics. Metabolomic analyses of larvae and adults have quantified cardenolide sequestration and detoxification, revealing how host-plant chemistry interacts with monarch genotype to shape toxin resistance and performance (Agrawal et al., 2012; Petschenka et al., 2013; Dreisbach et al., 2023). Population genomic resequencing across migratory and resident populations has identified loci associated with neural, metabolic, and endocrine function, providing candidates for functional validation (Zhan et al., 2014).

Genome editing approaches, including TALENs and CRISPR/Cas9, have enabled direct tests of gene function in monarchs and related Lepidoptera, allowing researchers to move from association-based inference toward causal understanding of traits such as circadian regulation and pigmentation (Markert et al., 2016; Zhang and Reed, 2016). Together, these monarch-focused functional and multi-omic applications illustrate how established technologies can be combined to address uniquely integrative questions spanning behavior, chemistry, and ecology.

3 Genetic Architecture of Migration and Seasonal Behavior

3.1 Migratory phenotype complexity

Monarch migration is a compound phenotype encompassing sun-compass orientation, reproductive diapause, lipid storage, flight endurance, and seasonal timing (Table 2). Sun-compass orientation depends on antennal circadian clocks and neural integration of solar cues, as demonstrated by experimental disruption of antennal function or clock genes (Merlin et al., 2009; 2020). Reproductive diapause is regulated by photoperiod and hormone signaling (Fleming and Alto, 2006; Green et al., 2019; Freedman et al., 2023), while lipid storage and flight endurance are shaped by metabolic and mitochondrial pathways associated with long-distance flight capacity (de Roode et al., 2011; Zhan et al., 2014). Seasonal timing of migration and breeding integrates environmental cues such as day length and temperature across generations. Collectively, these traits arise from interacting circadian, endocrine, metabolic, neural, and developmental modules, reflecting a modular and polygenic architecture underlying the monarch's migratory phenotype.

3.2 Antennal clocks, sun-compass orientation, and molecular candidates

Peripheral circadian clocks located in the antennae are essential for time-compensated sun-compass navigation, allowing monarchs to adjust orientation as the solar position changes throughout the day (Merlin et al., 2009; Hemstrom et al., 2025). These clocks interact with central brain regions involved in spatial and sensory integration, including the central complex and optic lobes (Merlin et al., 2009; Guerra et al., 2012). Core clock genes (e.g., *period*, *timeless*, *cryptochromes*) coordinate rhythmic gene expression underlying behavioral timing, while transcriptomic analyses implicate broader networks of sensory and metabolic genes contributing to energy allocation and flight performance (Zhan et al., 2011; Zhan and Reppert, 2013). Together, these findings highlight migration as an emergent property of interconnected circadian, sensory, and metabolic pathways rather than a single master regulator.

3.3 Population genomics: migratory vs. resident populations

Comparative genomic analyses of migratory and resident monarch populations reveal modest but consistent differentiation at loci associated with neural signaling, lipid metabolism, and endocrine function, consistent with adaptation to migratory versus sedentary lifestyles (Zhan et al., 2014; de Roode et al., 2013). Divergence at endocrine-related loci involved in juvenile hormone signaling may contribute to differences in reproductive diapause between populations (Hemstrom et al., 2025). Most signals are dispersed across the genome, supporting a largely polygenic architecture for migration, although a small number of loci with larger effect sizes may disproportionately influence key migratory traits (Freedman and Kronforst, 2023).

3.4 Toward causal tests

Advances in genomic mapping, selection experiments, and functional genetic approaches provide promising avenues for testing causal links between genotype and migratory phenotypes. Genome-wide association studies, artificial selection lines, and pedigreed crosses can be combined with CRISPR/Cas9-based validation to interrogate candidate genes involved in circadian regulation, sensory processing, and energy metabolism (Di