

## ECOLOGICAL GENOMICS

# Genomic signals of selection predict climate-driven population declines in a migratory bird

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The ongoing loss of biodiversity caused by rapid climatic shifts requires accurate models for predicting species' responses. Despite evidence that evolutionary adaptation could mitigate climate change impacts, evolution is rarely integrated into predictive models. Integrating population genomics and environmental data, we identified genomic variation associated with climate across the breeding range of the migratory songbird, yellow warbler (*Setophaga petechia*). Populations requiring the greatest shifts in allele frequencies to keep pace with future climate change have experienced the largest population declines, suggesting that failure to adapt may have already negatively affected populations. Broadly, our study suggests that the integration of genomic adaptation can increase the accuracy of future species distribution models and ultimately guide more effective mitigation efforts.

**A**nthropogenic climate change is having a marked impact on Earth's biodiversity (1). Rapid fluctuations in temperature and precipitation can alter the suitability of particular regions and in some cases, exceed the physiological limits of organisms (2, 3). The mismatch between environment and physiology can lead to shifts in species ranges, population declines, or even extinction (4–6). The difference between these evolutionary outcomes can in part be determined by the adaptive capacity of a species; those that possess standing genetic variation for climate-related traits are most likely to have the ability to adapt to rapidly changing environments (7, 8). Understanding the effects and distributions of potentially adaptive alleles associated with climate can therefore aid efforts to accurately predict species responses to future conditions (9), and aid in mitigation efforts.

Although migratory birds are highly sensitive to climate change (10–12), little is understood about how populations differ in adaptive capacity. Breeding ranges of North American migrants have shifted northward (13), but microevolutionary responses associated with these shifts remain poorly documented. Although genome-wide associations with climate variables have been shown to affect many groups across the tree of life (14–16), in migratory species it is less clear to what extent

genomic variation is shaped by environmental variables. Here, we examined the genomic basis of climate adaptation in a North American migratory bird, the yellow warbler (*Setophaga petechia*). Yellow warblers have a broad breeding range across the United States and Canada and are common throughout their range, though they have experienced local population declines and, in some regions, are listed as a species of concern (17). Because of their broad distribution, yellow warblers inhabit a large range of environmental conditions, making them an ideal system for investigating variation in local climate adaptation.

We used restriction site-associated DNA sequencing (RAD-Seq) to test for signals of selection across the breeding range. We examined 104,711 single-nucleotide polymorphisms (SNPs) in 229 individuals from 21 locations (table S1 and fig. S1), using our assembly of the first yellow warbler genome (18). Pairwise genetic distance between locations ( $F_{ST}/1 - F_{ST}$ ) was highly correlated with geographic distance, suggesting a strong signal of isolation by distance (Fig. 1A: Mantel's  $r = 0.85$ ,  $P = 1 \times 10^{-5}$ ), consistent with previous findings using microsatellite loci (19). Analysis of population structure using ADMIXTURE found little evidence of substructure, consistent with strong isolation by distance (fig. S2). Genetic distance was also significantly associated with environmental distance, based on climate variables, vegetation indices, and elevation, downloaded from public environmental databases (Fig. 1B: Mantel's  $r = 0.36$ ;  $P = 0.0006$ ). In a multiple regression of distance matrices, only geographic distance was significant (MRM:  $R^2 = 0.73$ ; geography  $P = 1 \times 10^{-5}$ ; environment  $P = 0.12$ ), suggesting that isolation by distance is the strongest force structuring genome-wide variation. This result is not unexpected, however, because environmental adaptation likely affects a small fraction of the genome (9). We used gradient forest (20), a

machine-learning regression tree-based approach, to test whether a subset of genomic variation can be explained by environment and to visualize climate-associated genetic variation across the breeding range (Fig. 1, C and D). Strong differences in environmentally associated genetic variation are apparent across longitude and latitude, and unique genotype-environment associations are present in the Rocky Mountains and Coastal British Columbia. Our results suggest that despite high dispersal capacity and vagility via annual migration, yellow warblers exhibit standing genetic variation associated with the environment among populations and are likely subject to environmentally mediated selection during the breeding season.

To investigate which populations might be most vulnerable to future climate change, we defined the metric “genomic vulnerability” as the mismatch between current and predicted future genomic variation based on genotype-environment relationships modeled across contemporary populations. We followed the method presented in Fitzpatrick and Keller (21) to calculate genomic vulnerability using an extension of the gradient forest analysis. Populations with the greatest mismatch are least likely to adapt quickly enough to track future climate shifts, potentially resulting in population declines or extirpations. Under future climate change scenarios [representative concentration pathways—RCPs—defined by the Intergovernmental Panel on Climate Change (22)], the regions with highest genomic vulnerability stretch from the southern Rocky Mountains to Alaska, along with patchy regions in the Eastern United States (Fig. 2A). As expected, genomic vulnerability increases under more severe climate change scenarios; under the most extreme scenario (RCP8.0), nearly the entire range is estimated to have high genomic vulnerability (fig. S4).

If future climate change is correlated with recent shifts (for example, if regional drying over the last century in some regions will continue and become more severe), we expect that recent climate change will have already negatively affected populations with high genomic vulnerability. We tested this idea by comparing genomic vulnerability scores (using 2050 RCP2.6, though the results were robust to different scenarios; fig. S4) to population trends estimated from North American Breeding Bird Surveys (23) (Fig. 2B). Regions that had higher genomic vulnerability scores experienced the largest population declines over the past half century [generalized additive model (GAM): adjusted  $R^2 = 0.101$ ;  $P < 0.001$ ; Fig. 2C], showing that populations already in decline are most vulnerable to future climate change and suggesting that a mismatch between genomic variation and climate may have already resulted in negative impacts. We believe that genomic vulnerability can therefore be used alongside other known causes of population decline, such as habitat degradation and avian disease, to understand and predict population dynamics.

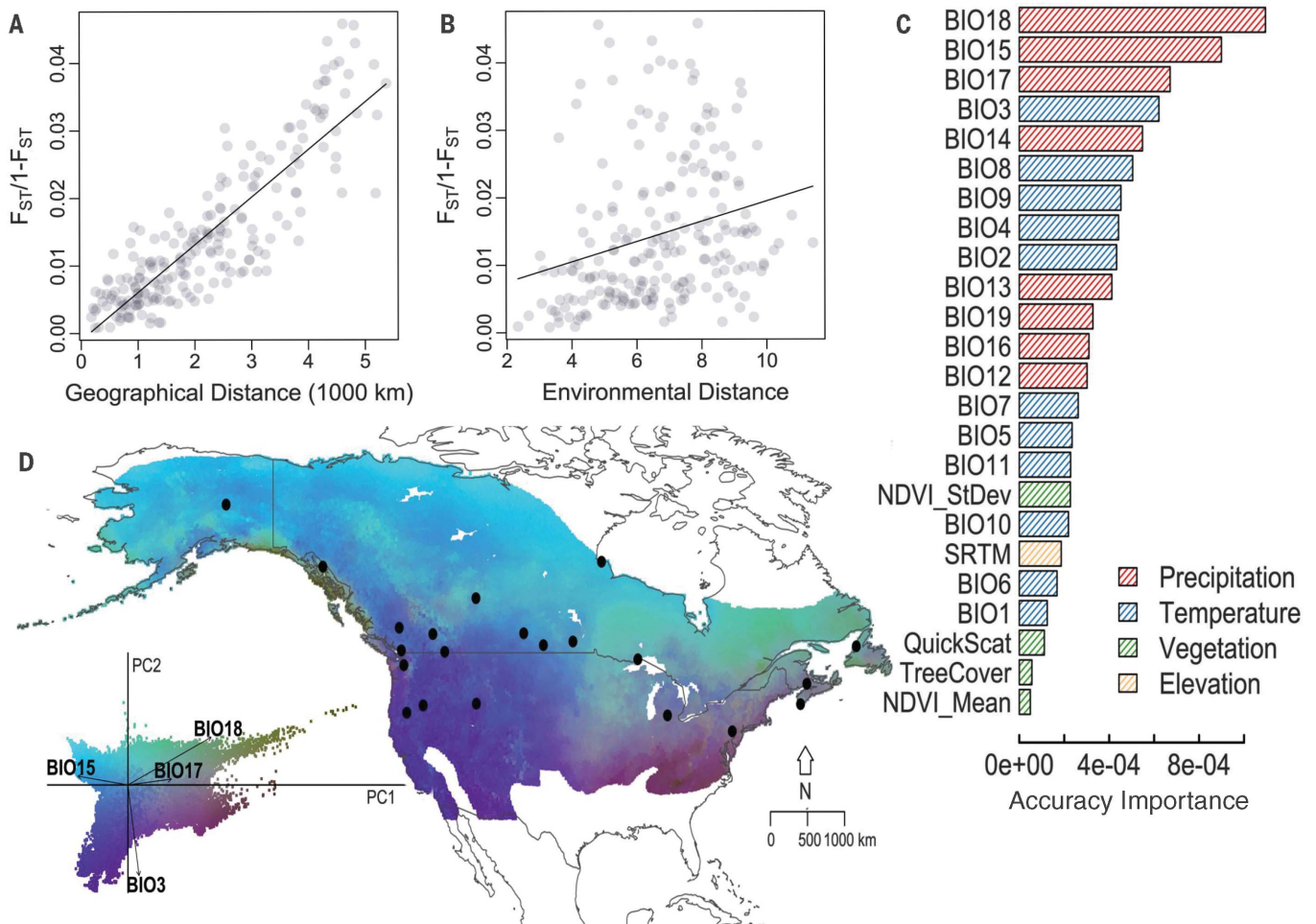
Understanding which environmental variables are most closely associated with local adaptation to particular climate conditions and vulnerability

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**Fig. 1. Geography and environment explain genomic variation in yellow warblers.** (A) Pairwise genetic distance ( $F_{ST}/1 - F_{ST}$ ) is associated with geographical distance and (B) environmental distance. (C) Ranked importance of environmental variables based on gradient forest analysis shows that climate, especially precipitation, strongly explains genomic variation.

(D) Gradient forest-transformed climate variables show climate adaptation across the breeding range. Colors are based on principal components analysis (PCA) of transformed climate variables [(D) inset: loadings of all variables are shown in fig. S3]. Points on map reflect sampled locations, and arrows on PCA show the loadings of top climate variables on PCA.

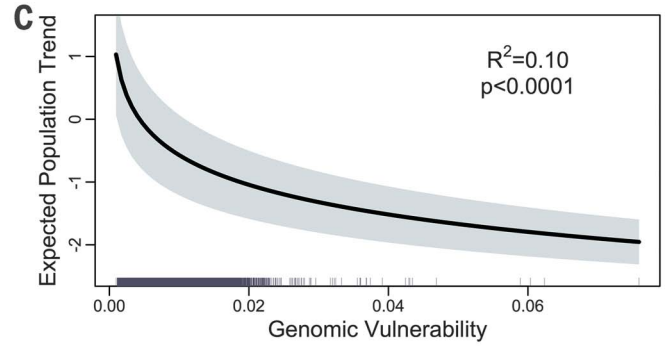
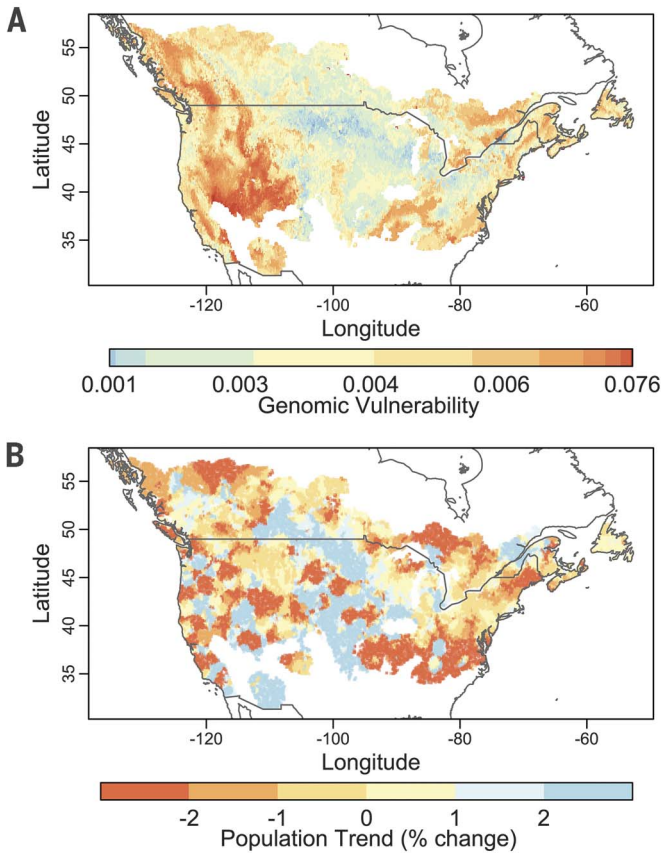
can prove useful in determining the biological mechanisms involved in population declines. Climate variables, especially precipitation measures, were most strongly associated with genomic variation across the breeding range of yellow warblers (Fig. 1C). Of the 25 environmental variables tested in the gradient forest analysis, the top three explanatory variables were precipitation related: (i) precipitation of the warmest quarter (BIO18), (ii) seasonality of precipitation (BIO15), and (iii) precipitation of the driest quarter (BIO17). Overall, precipitation variables were most important, followed by temperature variables and to a lesser extent, vegetation and elevation variables, suggesting that adaptation to precipitation is important on the breeding grounds.

To investigate the genomic basis of adaptation across contemporary climate gradients, we identified genomic regions associated with the top precipitation-related variables using latent factor mixed models (LFMMs) (24), which test for associations between genotypes and environments

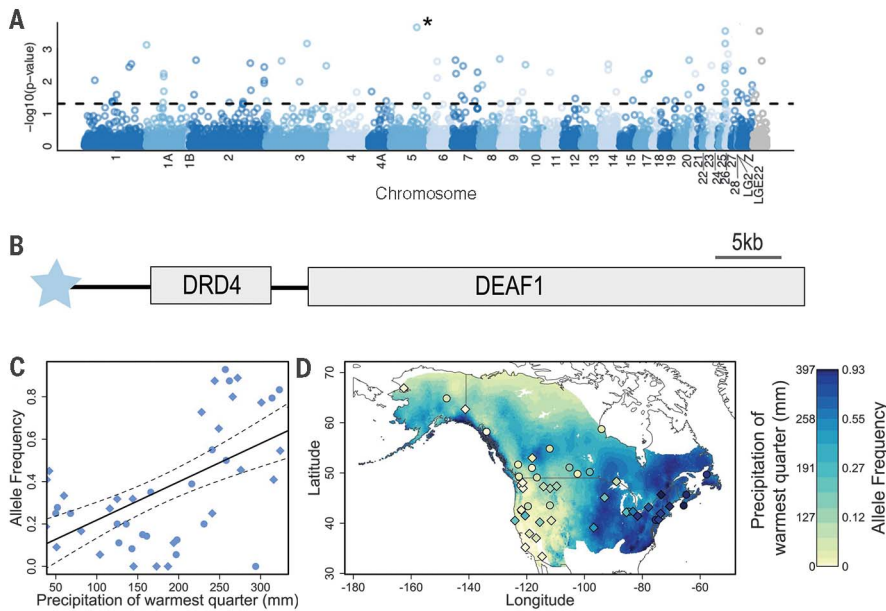
while accounting for background population structure (Fig. 3A and fig. S5). We found 85, 67, and 35 SNPs associated with climate variables BIO18, BIO15, and BIO17 (described above), respectively [false discovery rate (FDR)-corrected  $P < 0.05$ ]. These SNPs were broadly distributed across the genome, on 27 chromosomes (table S2). For the 13 SNPs associated with all three variables, we identified 12 adjacent genes with a range of functions including zinc finger genes (*ZNF397* and *ZKscan1*), peptide secretion (*SCT* and *MUCA*), and transmembrane proteins (*CDHR5*, *SLC25A33*, and *TEMEM201*). Targeted genotyping using Fluidigm assays for 17 SNPs associated with climate in the LFMM analysis in an additional 309 birds at 29 locations independently validated climate associations in 8 out of 17 SNPs (FDR-corrected  $P < 0.05$ ; table S3) with marginal associations in an additional two SNPs (FDR-corrected  $P < 0.1$ ).

One of the strongest associations between genotype and climate was upstream of genes with known function in avian behavior and migration. A SNP on chromosome 5 was very strongly

associated with all three top environmental variables (LFMM  $P < 0.001$ ; Fig. 3), and these associations were validated with Fluidigm assays ( $P < 0.001$ ; Fig. 3, C and D). The highest allele frequencies at this SNP occurred in the Maritime provinces of Canada (Nova Scotia and Newfoundland), areas of high rainfall and low seasonality. This SNP is upstream of two genes, *DRD4* and *DEAF1* (Fig. 3B), that have known associations with migration in birds (25, 26). The *DRD4* gene in particular, a dopamine receptor, has been extensively studied for its involvement in novelty-seeking behavior in primates, fish, and birds (26). Polymorphisms in this gene are linked to novelty-seeking or exploratory behavior in a number of bird species (27, 28), and linkage blocks extend into the neighboring *DEAF1* gene, a transcription factor involved in serotonergic signaling. The exploratory phenotype has been linked to dispersal, which is thought to allow species to occupy new environments (25), but experimental studies linking behavior, genotype, and environment are needed to fully understand how these variants might



**Fig. 2. Genomic vulnerability to future climate change is associated with a higher probability of population decline.** (A) Genomic vulnerability based on 2050 RCP2.6 projections. (B) Population trend estimates (percent change per year) for yellow warblers based on North American Breeding Bird Survey analysis (23). (C) Generalized additive model (GAM) showing the relationship between population trend and predicted genomic vulnerability. The black line represents the model fit, and the shaded area is the 95% confidence interval.



**Fig. 3. Genome-wide variation associated with climate variables.** (A) Manhattan plots show the significance level (FDR-corrected) for SNP associations with precipitation of the warmest month (BIO18). Dashed line represents  $P = 0.05$ . Colors distinguish different chromosomes, and gray points are SNPs not anchored to a chromosome. (B) The most significant SNP association, marked with an asterisk (\*) in (A), is upstream from the *DRD4* and *DEAF1* genes. (C and D) Correlations between allele frequency and BIO18 for this SNP. Samples genotyped by RAD-Seq are represented as circles, and samples genotyped with Fluidigm assays are shown as diamonds.

be involved in climate adaptation. However, this SNP represents a single locus with significant associations between genotype and environment, but many other highly significant candidates exist (table S2), highlighting the complex and polygenic nature of climate adaptation.

Expected patterns of environmentally mediated evolution in migratory animals are complex but could drastically alter predictions of species response to climate change. We showed that standing variation for adaptation to different climate regimes exists and that natural selection during breeding months is driving evolutionary

shifts in the genome. High genomic vulnerability, or mismatch between current allelic variation and future environmental conditions, was correlated with a higher likelihood of population decline, suggesting that yellow warbler populations may have already experienced some negative impacts of climate change over the past 50 years.

Our results show how the integration of genomic, environmental, and demographic data can provide a more thorough understanding of future climate change impacts on a migratory bird species. More broadly, we illustrate a new approach for understanding climate-associated causes of current and future declines and an important tool for making more-informed conservation decisions.

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#### SUPPLEMENTARY MATERIALS

www.sciencemag.org/content/359/6371/83/suppl/DC1  
Materials and Methods  
Figs. S1 to S7  
Tables S1 to S3  
References (29–48)

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## Genomic signals of selection predict climate-driven population declines in a migratory bird

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### Yellow warblers already in decline

As the climate changes, species' ability to adapt to changing conditions may relate directly to their future persistence. Determining whether and when this will happen is challenging, however, because it is difficult to tease apart the causes of decline or maintenance. Bay *et al.* looked at the relationship between genomic variation and the environment in North American populations of the yellow warbler (see the Perspective by Fitzpatrick and Edelsparre). Genes linked to exploratory and migratory behavior were important for successful climate adaptation. Furthermore, populations identified as "genetically vulnerable" because of limited climate-associated genomic variation were already declining.

*Science*, this issue p. 83; see also p. 29

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## EVOLUTION

# The genomics of climate change

A study of yellow warblers identifies genomic regions involved in climate change adaptation

By **Mark J. Fitzpatrick** and **Allan H. Edelsparre**

**H**uman-induced climate change is causing rapidly changing global temperatures and extreme fluctuations in precipitation. These changes force organisms to adapt and evolve or face extinction. Understanding and predicting the evolutionary responses to climate change is critical for preserving biodiversity, but predictions are challenging because they involve interactions between adaptive plasticity (such as altered breeding times) and evolved responses (such as increased metabolism). On page 83 of this issue, Bay *et al.* (1) combine high-resolution genomic sequencing with population trends and global climate predictions to estimate the adaptive potential (that is, the genetic

variation necessary for adaptation) of yellow warblers (see the photo) to climate change and predict future population declines. In doing so, they produce a powerful tool for estimating genomic vulnerability to climate change and locate candidate genes that are key for climate change adaptation.

Yellow warblers are migratory birds with a wide distribution across North America. They occupy a rich set of habitats that range from marshes and forests to urbanized areas. They can be found in lowlands as well as at high altitudes, such as in the Rocky Mountains in the west and the Appalachian Mountains in the east. Given their wide distribution and general abundance, recent declines of some populations have raised concerns that yellow warblers may be negatively affected by climate change (2).

Bay *et al.* initially obtained DNA samples from 229 birds, representing 21 populations that span the yellow warbler breeding range. They used more than 100,000 nucleotide markers [single-nucleotide polymorphisms

(SNPs)] to characterize the statistical associations between current population-level genetic variation and 25 environmental variables associated with climate change. The variables included factors associated with precipitation, temperature, elevation, tree cover, and vegetation. The strongest associations between genomic and environmental variation were those related to precipitation. This makes sense, because changes in precipitation directly influence biomass, which in turn affects other factors, such as shelter and food availability. Extreme changes in precipitation remain among the most important, but least understood, consequences of rising temperatures across the globe (3).

By extracting information from their assembly of the yellow warbler genome, the authors assessed the adaptive potential of each population by piecing together a portrait of genomic regions that respond to climate-related changes and then searched for traces of selection in those regions. One

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major advantage to teasing out the adaptive potential from standing genetic variation is that it gives us the ability to ask whether such information can be used to forecast climate-related declines. By comparing the genometrically determined adaptive potential of each population with local climate-related variables, Bay *et al.* were able to determine which populations have the greatest mismatch with their environment (as determined by the degree to which their genomic variation matches the environmental variation they experience), a metric they refer to as genomic vulnerability.

The most vulnerable populations largely reside along the Rocky Mountains, a region particularly affected by droughts over the past decade (4). The authors determined that these vulnerable populations coincide with recent population declines reported in the literature (5). This link between genomic vulnerability scores and realized population trends strongly suggests that genomic vulnerability accurately forecasts which popula-

### “...behavioral genes may represent ‘first responders’ to climate change adaptation.”

tions may be at risk of declining. This allows conservation efforts to target these identified areas and populations before environmental conditions become unsustainable.

The estimates of adaptive potential within species can be used to identify the traits and genes influenced by climate change. To do so, Bay *et al.* took a closer look within the important genomic regions discussed above. They found a strong association between climate (e.g., precipitation) and a SNP marker on chromosome 5, located very close to *DRD4* and *DEAF1*; these two genes were previously linked with migration and exploratory behavior in several species, including birds (6) and humans (7). Initial responses to climate change likely involve highly plastic traits like behavior, where individuals themselves can act to better match their current environmental conditions; examples include avoidance behavior, retreating or reclaiming new habitats, diet modifications, dispersal, and migration.

Although the direct involvement of *DRD4/DEAF1* needs to be established, their potential role in climate change adaptation is intriguing and raises the possibility that behavioral genes may represent “first responders” to climate change adaptation. If these adaptations involve dietary changes, dispersal, and migration, then additional candidate genes may include

*Pgi* (8), *npr-1* (9), and *foraging* (10), all of which have been associated with food search and dispersal.

Identifying general features of evolutionary responses to climate change is a crucial, but intricate, mission. Climate-driven adaptations will necessarily involve the genome, but time- and context-dependent factors will likely influence the specific pathway that any given population takes (including extinction). Some scenarios will directly lead to the evolution of new/modified alleles, whereas other scenarios may exist without any traditional genomic responses but instead be regulated by factors such as adaptive plasticity and epigenetics. The latter is particularly interesting, because both *DRD4* (11) and *foraging* (12) can be regulated epigenetically to produce variations in behavioral tendencies that underlie food-searching and exploratory strategies within populations.

Climate change is happening and, despite growing global concern, is predicted to progress (13). Bay *et al.*'s study of the yellow warbler shows that, although populations can evolve in response to climate change, this response is limited by the adaptive potential and genomic vulnerability found among populations. A critical next step will be to determine how broadly these findings apply to other species and communities, especially those that are highly threatened. Time is of the essence. The widespread impact of climate change on our ecosystems and biodiversity has occurred over a relatively short time scale (about 50 years). According to the global forecasts of future climate change, the pervasive impact and strain on biodiversity will only intensify (3). ■

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#### CELL BIOLOGY

## A new mitotic activity comes into focus

The ATR kinase has a role in mitosis to promote chromosome segregation

By Joshua C. Saldivar and Karlene A. Cimprich

During mitosis, each duplicated chromosome must be accurately attached to the microtubule spindle, which pulls the chromosomes to opposite poles of the cell, where they are segregated to daughter cells. A number of mitotic kinases orchestrate mitosis to ensure accurate segregation, including cyclin-dependent kinase 1 (CDK1), the Polo-like kinases, and the Aurora kinases (1). The kinase ATR (ataxia telangiectasia and Rad3-related), which is involved in DNA damage responses during interphase of the cell cycle, has also been shown to prevent chromosome segregation errors (2). However, this role of ATR was presumed to be an indirect effect. On page 108 of this issue, Kabeche *et al.* (3) unveil a mitosis-specific ATR activity that ensures proper chromosome segregation and that this activity is dependent on a specific three-stranded nucleic acid structure known as an R loop.

ATR is a master regulator of the cellular responses to DNA damage and DNA replication stress by controlling cell-cycle progression, replication origin firing, replication fork stability, and DNA repair (4). These functions are mediated by the kinase activity of ATR and safeguard genome integrity. Kabeche *et al.* found that ATR is localized to and active at mitotic centromeres, the chromosomal region where the microtubule spindle attaches (see the figure). Because no mitosis-specific function of ATR was previously known, this is an intriguing observation.

Microtubules of the mitotic spindle attach to kinetochores at centromeres to facilitate chromosome segregation (5). Given the local activation of ATR at the centromeres of mitotic chromosomes, the authors assessed chromosome segregation

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