the case of antibodies, by contrast, the structural independence of V and C domains (*28*), together with the much larger separation expected between the V domains and putative signal-transducing molecules on the cell surface (*30*), effectively rules out an allosteric mechanism to account for B cell activation. In this respect, the large protruding loop on the external face of the C_β domain (and possibly of the C_γ domain), comprising residues 219 to 232 (Fig. 1), could be particularly important in contacting the extracellular portions of CD3 molecules, thereby helping to couple the antigen recognition and signal transduction functions of the TCR-CD3 complex.

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6. We initially obtained crystals of a glycosylated form of the 14.3.d β chain (*26*). As these diffracted only to medium resolution, however, site-directed mutagenesis was used to eliminate four out of the five potential NH_2-linked glycosylation sites. Asparagines at positions 24, 74, and 121 were mutated to glutamine, and Ser^{283}, which is COOH-terminal to Asn^{236}, was mutated to valine. The prototype vector containing immunoglobulin locus elements (*31*) was used to drive expression of the mutated complementary DNA corresponding to the rearranged V_β and the first C region exon of the TCR β gene. Soluble β chain was produced in myeloma cells and purified from culture supernatants (~10 mg/ml) by a single affinity chromatography step with the C_β monoclonal antibody H57-597 (*32*). The unmutated NH_2-linked glycosylation site at position 186 was used only in a few of the chains (<10%), as judged by SDS–polyacrylamide gel electrophoresis. A homogeneous product was obtained by treatment of the native protein with neuraminidase and glycosidases.
7. Protein solution [5.8 mg/ml in 7.3 mM tris, 25 mM Hepes (pH 7.5), 18.3 mM NaCl, 1.0% (w/v) polyethylene glycol (PEG) 4000, 0.75% (saturated) ammonium sulfate, and 0.014% agarose] was used to form a sitting drop, which was equilibrated by vapor diffusion over a buffer reservoir of higher concentration (4% PEG 4000, 0.1 M Hepes, and 3% ammonium sulfate at pH 7.25). Crystals (0.4 mm by 0.4 mm by 0.1 mm) usually grew within a period of about 3 weeks. They belong to the space group C2 with unit cell parameters a = 100.6 Å, b = 36.6 Å, c = 71.5 Å, and β = 113.4°.
8. A data set was collected with a MARresearch (Hamburg, Germany) imaging plate system mounted on the wiggler line DW32 at the synchrotron at LURE (Laboratory for the Utilization of Electromagnetic Radiation), Orsay, France. A total of 60,827 reflections were obtained from a single crystal to yield a set of 25,371 unique observations (R_{sym} = 0.049), which was 95.6% complete at a resolution between 15.0 and 1.7 Å. (For the outer resolution shell, 1.76-1.70 Å, R_{sym} was 0.399 with 95.1% completeness and 34% having I > 3σ.) A preliminary model for the β chain was obtained by molecular replacement with the program AMoRe (*33*) with V_L from HyHEL-10 (*12*) and C_H1 as search models. The structure was refined with the program X-PLOR (*34*) during the preliminary stages, then with the CCP4 (*35*) version of PROLSQ (*36*) for

the final steps. The R factor of the refined model is 0.198 for 21,745 reflections, with F > 3σ in the resolution range of 7.0 to 1.7 Å (0.208 for all 23,577 reflections in this resolution range). The rms deviations of bonds and angles from the target values are 0.013 Å and 2.0°, respectively. The final model of the β chain included all 238 residues in the main chain trace of the recombinant molecule and 107 solvent molecules.
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Regional Forest Fragmentation and the Nesting Success of Migratory Birds

Scott K. Robinson,* Frank R. Thompson III, Therese M. Donovan, Donald R. Whitehead, John Faaborg

Forest fragmentation, the disruption in the continuity of forest habitat, is hypothesized to be a major cause of population decline for some species of forest birds because fragmentation reduces nesting (reproductive) success. Nest predation and parasitism by cowbirds increased with forest fragmentation in nine midwestern (United States) landscapes that varied from 6 to 95 percent forest cover within a 10-kilometer radius of the study areas. Observed reproductive rates were low enough for some species in the most fragmented landscapes to suggest that their populations are sinks that depend for perpetuation on immigration from reproductive source populations in landscapes with more extensive forest cover. Conservation strategies should consider preservation and restoration of large, unfragmented "core" areas in each region.

The conservation of neotropical migrant bird species, which breed in North America and winter in the tropics, has attracted attention even though most are not yet endangered (*1*, *2*). Many neotropical migrants, however, are suffering population declines, the causes for which may include the loss of breeding, wintering, and migra-

tion stopover habitats (*3*). A frequently hypothesized cause for declines in populations of migrant birds is the negative impact of habitat fragmentation (*4*) on breeding success (*5*). Habitat fragmentation may allow higher rates of brood parasitism by brown-headed cowbirds (*Molothrus ater*) and nest predation (*6*, *7*). Cowbirds lay their eggs in the nests of other "host" species, which then raise cowbirds at the expense of their own young (*8*).

Populations of cowbirds and many nest predators are higher in fragmented landscapes where there is a mixture of feeding habitats (agricultural and suburban) and breeding habitats (forests and grasslands) (*8–10*). In landscapes fragmented by agri-

S. K. Robinson, Illinois Natural History Survey, 607 East Peabody Drive, Champaign, IL 61820, USA.
F. R. Thompson III, North Central Forest Experiment Station, University of Missouri, Columbia, MO 65211, USA.
T. M. Donovan and J. Faaborg, Division of Biological Sciences, University of Missouri, Columbia, MO 65211, USA.
D. R. Whitehead, Department of Biology, Indiana University, Bloomington, IN 47405, USA.

*To whom correspondence should be addressed.

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cultural fields, levels of nest predation and brood parasitism are so high that many populations of forest birds in the fragmented landscapes are likely to be population "sinks" (11) in which local reproduction is insufficient to compensate for adult mortality (12). As landscapes become increasingly fragmented, this reproductive dysfunction could cause regional declines of migrant populations (7).

Previous studies of the effects of fragmentation have focused primarily on reproductive success as a function of local factors such as habitat size or distance to the habitat edge (5, 13). Many studies used artificial nests (14), which may not reflect natural predation levels (15), or relied on composite data from natural nests of many host species (6, 7, 16, 17).

We tested the hypothesis that the reproductive success of nine species of forest birds was related to regional (midwestern United States) patterns of forest fragmentation. We measured nest predation and brood parasitism in nine different landscapes ranging from over 90% agricultural to more than 90% forested. The study areas were in Illinois, Indiana, Minnesota, Missouri, and Wisconsin.

This study involved the coordinated efforts of five teams of 5 to 25 researchers (totaling over 100 assistants) who located and monitored the fates of more than 5000 nests on nine study areas from 1989 to 1993. The study areas represented the entire range of forest fragmentation available in the Midwest (Fig. 1). Each study area consisted of two to nine sites on which nests were monitored every 2 to 7 days to determine if they were parasitized and to calculate the daily predation rate with the Mayfield index (18). Data were pooled from nests in all years and on all sites within a study area (19). Comparing parasitism and predation levels from different years could result in errors, but these should be minimal

because most of the study area estimates are means from several years with an overlap in years among study areas. We include data from nine species for which we have data from at least four sites (20). All species except the northern cardinal are neotropical migrants.

We constructed a map of forest cover for the entire region from 1:250,000 scale digital land use and land cover data derived from thematic overlays (21). A spatial analysis program (FRAGSTATS) (22) was used to calculate the mean percent forest cover, mean percent forest interior (forest >250 m from an edge), and mean forest patch size within a 10-km radius of the center of each site. We then calculated means for the forest statistics from all of the sites within a study area (Fig. 2). For each species, we calculated Pearson correlation coefficients for the relation of the daily nest mortality and percent nests parasitized with the percent forest cover, percent forest interior, and mean forest patch size. We tested the hypothesis that brood parasitism and nest predation were related to the forest cover statistics for all species by combining the probabilities from the species-specific correlations (23). The forest cover statistics were log-transformed when necessary. Percent forest cover, percent forest interior, and mean forest patch size were all highly correlated [all correlations were significant at the 0.001 level, correlation coefficient $(r) = 0.89$ to 0.985]. We only present results for percent forest cover because it had the highest correlations with nesting success for most species.

Cowbird parasitism was negatively correlated with percent forest cover for all species; correlations were significant [probability $(P) \leq 0.05$] for five of the nine species studied (Fig. 3). The combined probabilities test (23) indicated that, overall, nest parasitism was significantly negatively related to the amount of forest cover

in the landscape ($P \leq 0.01$). Most wood thrush nests in landscapes with less than 55% forest cover were parasitized. In some landscapes, there were more cowbird eggs than wood thrush eggs per nest (11). In contrast, cowbird parasitism levels were so low in the heavily forested landscapes that cowbird parasitism is unlikely to be a significant cause of reproductive failure (24).

There were some exceptions to the trends. Parasitism levels were consistently higher in the four Illinois sites than in comparably fragmented forests in the other states. Cowbird abundance was also higher in the Illinois landscapes (10). Several migrant species were heavily parasitized in the mostly forested Indiana landscape where most other species were rarely parasitized. These results suggest that local factors such as the spatial distribution and kinds of forest edges, the quality of cowbird feeding areas, and preferences by cowbirds for particular hosts also influence parasitism.

Levels of nest predation also declined with increasing forest cover for all species. Although only three of the nine species had a significant ($P \leq 0.05$) negative correlation with percent forest cover (Fig. 4), the combined probabilities test for the overall effect across all species was significant ($P < 0.02$). Three ground-nesting warblers (the ovenbird and the worm-eating and Kentucky warblers) and two species that nest near the ground in shrubs (hooded warbler and indigo bunting) all had extremely high (6% or higher) daily predation rates in the most

Fig. 1. Distribution of forest habitat in the midwestern United States and locations of the study areas. Abbreviations: CAIL, Cache River, Illinois; CNIL, central Illinois; NCMO, north-central Missouri; NWIL, northwestern Illinois; NWWI, northwestern Wisconsin; SCMO, south-central Missouri; SOIN, southern Indiana; SWIL, southwestern Illinois; and WCWI, west-central Wisconsin.
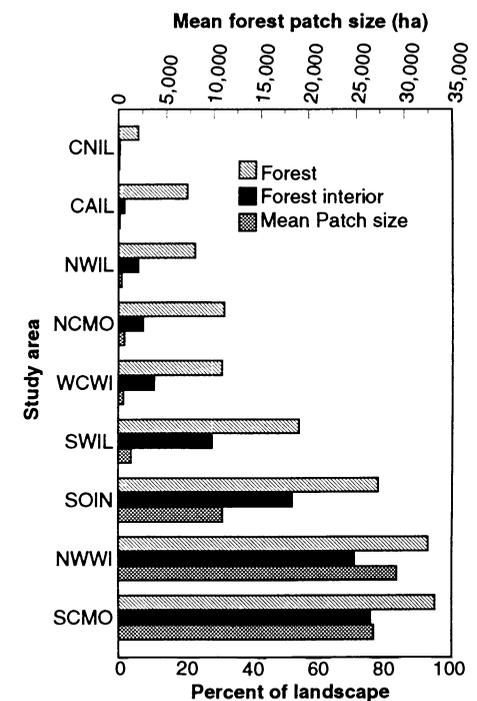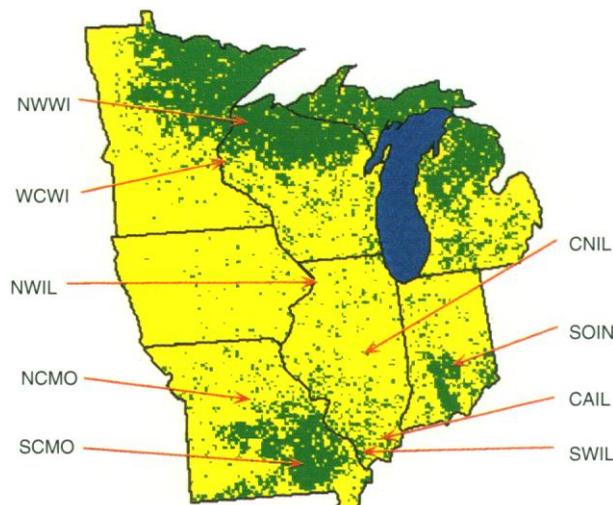

Fig. 2. Forest cover statistics for the nine study areas (landscapes) shown in Fig. 1 in the midwestern United States. Abbreviations as in Fig. 1.

fragmented landscapes. Twelve of the 13 cases of daily predation rates exceeding 7% (>80% of all nests lost to predators) were in the four most fragmented landscapes.

Fragmentation at the landscape scale thus affects the levels of parasitism and predation on most migrant forest species in the midwestern United States. Even the indigo bunting, which prefers forest edges (5), nests more successfully in less fragmented landscapes. Cowbirds can commute up to 7 km between breeding and feeding areas and therefore use widely scattered feeding areas (25). The scale (10-km radius around each study area) on which we measured forest fragmentation is appropriate because it is similar in size to the home ranges of cowbirds. In heavily forested landscapes, cowbird populations may be more limited by the availability of foraging areas than by host availability. In more fragmented landscapes, on the other hand, the cowbird populations may be more limited by the

availability of hosts and may saturate the available breeding habitat, which would result in high levels of parasitism even in the interior (>600 m from the forest edges) of the largest (up to 2200 ha) tracts in Illinois (10). Therefore, landscape-level factors such as percent forest cover determine the magnitude of local factors such as tract size and distance from the forest edges, a result consistent with continental analyses of parasitism levels (25).

Nest predators such as mammals, snakes, and blue jays (Cyanocitta cristata) likely have smaller home ranges than cowbirds (26) and may therefore be more affected by local than by landscape-level habitat conditions. Small woodlots in agricultural landscapes, for example, have high populations of raccoons (Procyon lotor) (27). Censuses in both Missouri and Wisconsin have shown blue jay and crow (Corvus brachyrhynchos) abundances to be much higher in fragmented regions (28). High predation rates of ground- and near-ground–nesting birds in the most fragmented landscapes may reflect the abundance of these predators (29). We know very little, however,

about how fragmentation affects populations of most nest predators.

The large differences between the levels of parasitism and predation in fragmented and unfragmented landscapes (Figs. 3 and 4) provide strong evidence that "source-sink" population models (12) may be applicable. Parasitism levels of wood thrushes, tanagers, and hooded warblers and predation rates on ovenbirds and Kentucky warblers were so high in the most fragmented forests that they are likely population sinks (28). Extensive forests of the Missouri Ozarks, northern Wisconsin, and south-central Indiana have low levels of nest predation and parasitism and may provide the surplus of colonists necessary to maintain populations in fragmented forests in southern Wisconsin, Illinois, and northern Missouri (30). Understanding source-sink population dynamics, however, requires data on the season-long productivity of females and dispersal distances and a better understanding of adult and juvenile mortality (24). Nevertheless, the persistence of migratory songbirds in areas of very low nesting success provides strong evidence for source-sink metapopulation structure (11).

Our results suggest that a good regional conservation strategy for migrant songbirds in the Midwest is to identify, maintain, and restore the large tracts that are most likely to be population sources. Further loss or fragmentation of habitats could lead to a collapse of regional populations of some forest birds (7, 30). Land managers should seek to minimize cowbird foraging opportunities within large, unfragmented sites (8, 10). In more fragmented landscapes, the reduction of cowbird parasitism may require trapping and large-scale restoration efforts (8), whereas reduction of local forest edges may reduce nest predation (14) and increase mating success (29, 31). As long as an adequate number of large, unfragmented regions remain in North America, it is unlikely that fragmentation alone will drive populations of migrant birds to extinction. Increasing fragmentation of landscapes, however, could be contributing to the widespread population declines of several species.
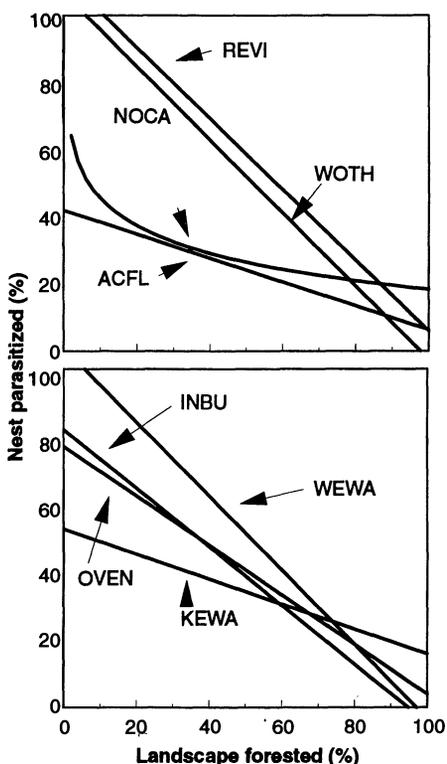

Fig. 3. Correlations between proportion of parasitized nests and percent forest cover in nine study areas (landscapes) in the midwestern United States. Abbreviations: ACFL, acadian flycatcher; INBU, indigo bunting; KEWA, Kentucky warbler; NOCA, northern cardinal; OVEN, ovenbird; REVI, red-eyed vireo; WEWA, worm-eating warbler; and WOTH, wood thrush. For species names, see (20). The statistics for each species are as follows: ACFL ($r = -0.66, P = 0.10$), INBU ($r = -0.97, P = 0.01$), KEWA ($r = -0.62, P = 0.19$), NOCA ($r = -0.69, P = 0.12$), OVEN ($r = -0.76, P = 0.05$), REVI ($r = -0.94, P < 0.01$), WEWA ($r = -0.97, P = 0.02$), and WOTH ($r = -0.92, P < 0.01$).
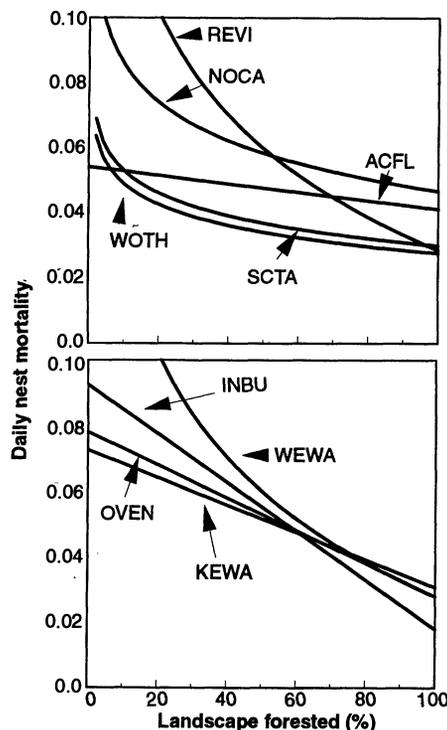

Fig. 4. Correlations between daily nest predation rate and percent forest cover in nine study areas (landscapes) in the midwestern United States. SCTA, scarlet tanager. Other abbreviations are as in Fig. 3. The statistics for each species are as follows: ACFL ($r = -0.12, P = 0.79$), INBU ($r = -0.82, P = 0.05$), KEWA ($r = -0.67, P = 0.14$), NOCA ($r = -0.47, P = 0.28$), OVEN ($r = -0.49, P = 0.21$), REVI ($r = -0.55, P = 0.19$), SCTA ($r = -0.49, P = 0.25$), WEWA ($r = -0.99, P = 0.01$), and WOTH ($r = -0.74, P = 0.02$).

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19. Study areas included northwestern Illinois (NWIL), five woodlots (90 to 525 ha) (1992–1993 only) in Jo Daviess and Carroll counties; central Illinois (CNIL), three woodlots (65 to 300 ha) in Shelby, Champaign, and Piatt counties; southwestern Illinois (SWIL), four areas in 1000- to 3500-ha tracts in the Shawnee National Forest and Trail of Tears State Forest in Union and Alexander counties; Cache River, IL (CAIL), six study sites in 25- to 1600-ha forests in the Cache River Bioreserve of Johnson, Union, Pulaski, and Alexander counties; southern Indiana (SOIN), four study sites (ranging from 133 to 190 ha) in a >40,000-ha forest tract in the vicinity of the Pleasant Run Unit of Hoosier National Forest of Monroe, Brown, Jackson, and Lawrence counties; northwestern Wisconsin (NWWI), six study areas within the Chequamegan National Forest, Bayfield County; west-central Wisconsin (WCWI), six study areas (80- to 160-ha patch size) along the St. Croix River in Washington and Chisago counties, MN, and Polk County, WI; south-central Missouri (SCMO), eight study areas within the contiguous Ozark Forests in Shannon, Reynolds, and Carter counties; north-central Missouri (NCMO), nine study sites within Boone, Callaway, and Randolph counties in tracts ranging from 150 to 900 ha.
20. Study species included the acadian flycatcher (ACFL) *Empidonax virescens*, wood thrush (WOTH) *Hylocichla mustelina*, red-eyed vireo (REVI) *Vireo olivaceus*, ovenbird (OVEN) *Seiurus aurocapillus*, worm-eating warbler (WEWA) *Helmitheros vermivorus*, Kentucky warbler (KEWA) *Oporornis formosus*, scarlet tanager (SCTA) *Piranga olivacea*, northern cardinal (NOCA) *Cardinalis cardinalis*, and indigo bunting (INBU) *Passerina cyanea*. Sample sizes per species ranged from 50 nests (SCTA) to over 500 (ACFL and WOTH).
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30. For source-sink models of the wood thrush and ovenbird in this landscape, see T. M. Donovan, R. H. Lamberson, F. M. Thompson III, J. Faaborg, *Conserv. Biol.*, in press; T. M. Donovan, F. R. Thompson III, J. Faaborg, J. Probst, *ibid.*, in press.
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Requirement of Serine Phosphorylation for Formation of STAT-Promoter Complexes

Xiaokui Zhang, John Blenis, Heng-Chun Li, Chris Schindler, Selina Chen-Kiang*

Members of the interleukin-6 family of cytokines bind to and activate receptors that contain a common subunit, gp130. This leads to the activation of Stat3 and Stat1, two cytoplasmic signal transducers and activators of transcription (STATs), by tyrosine phosphorylation. Serine phosphorylation of Stat3 was constitutive and was enhanced by signaling through gp130. In cells of lymphoid and neuronal origins, inhibition of serine phosphorylation prevented the formation of complexes of DNA with Stat3-Stat3 but not with Stat3-Stat1 or Stat1-Stat1 dimers. In vitro serine dephosphorylation of Stat3 also inhibited DNA binding of Stat3-Stat3. The requirement of serine phosphorylation for Stat3-Stat3·DNA complex formation was inversely correlated with the affinity of Stat3-Stat3 for the binding site. Thus, serine phosphorylation appears to enhance or to be required for the formation of stable Stat3-Stat3·DNA complexes.

The Janus kinase (Jak)–STAT pathway transduces the signals of many cytokines and peptide growth factors (*1*). Ligand binding rapidly triggers tyrosine phosphorylation of STATs (*2, 3*) by receptor-associated Jak family tyrosine kinases (*4, 5*). The activated STATs dimerize and translocate into the nucleus, where they directly activate target genes by binding to specific promoter sequences (*1*). The pleiotropic cytokines interleukin-6 (IL-6), ciliary neuro-

trophic factor (CNTF), leukemia inhibitory factor (LIF), oncostatin M, and IL-11 transduce signals through gp130, a common component of the receptor complexes (*6, 7*). IL-6 primarily activates Stat3 [also known as acute-phase response factor (APRF)] (*8, 9*) in the liver (*9, 10*), but it also activates Stat1 (*11*) in human hepatoblastoma HepG2 cells (*8, 12, 13*). Signaling by CNTF activates Stat1 and two Stat1-related proteins in a human neuroblastoma cell line SK-N-MC (*14*). Activated Stat3 and Stat1 form three distinct protein-DNA complexes that contain either Stat1 homodimers, Stat1-Stat3 heterodimers, or Stat3 homodimers when they bind to the Stat-binding site present in the c-*fos* promoter (*8, 12, 13, 15*). Studies of the activation of Stat1 by interferon γ (IFN-γ) suggest that Stat1 can form stable dimers by interactions between the Src homology 2

X. Zhang and S. Chen-Kiang, Brookdale Center for Molecular Biology, Mount Sinai School of Medicine, New York, NY 10029, USA.
J. Blenis, Department of Cell Biology, Harvard Medical School, Boston, MA 02115, USA.
H.-C. Li, Department of Biochemistry, Mount Sinai School of Medicine, New York, NY 10029, USA.
C. Schindler, Department of Medicine, College of Physicians and Surgeons, Columbia University, New York, NY 10032, USA.

*To whom correspondence should be addressed.