on by climate changes and allowed them to coalesce, potentially leading to the eventual regime shifts and collapses observed in megafaunal ecosystems. The lack of evidence for larger-scale ecological regime shifts during earlier periods of the Glacial (i.e., >45 ka) when interstadial events were common, but modern humans were not, supports a synergistic role for humans in exacerbating the impacts of climate change and extinction in the terminal Pleistocene events.

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Impairment of immunity to Candida and Mycobacterium in humans with bi-allelic RORC mutations

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Human inborn errors of immunity mediated by the cytokines interleukin-17A and interleukin-17F (IL-17A/F) underlie the candidiasis, whereas inborn errors of interferon-γ (IFN-γ) immunity underlie mycobacterial disease. We report the discovery of bi-allelic RORC loss-of-function mutations in seven individuals from three kindreds of different ethnic origins with both candidiasis and mycobacteriosis. The lack of functional RORγT and RORγT isoforms resulted in the absence of IL-17A/F-producing T cells in these individuals, probably accounting for their chronic candidiasis. Unexpectedly, leukocytes from RORγT RORγT-deficient individuals also displayed an impaired IFN-γ response to Mycobacterium. This principally reflected profoundly defective IFN-γ production by circulating γδ T cells and CD4⁺CCR6⁺CXCR3⁺ γδ T cells. In humans, both candidiasis immunity to Candida and systemic immunity to Mycobacterium require RORγT, RORγT, or both.

Inborn errors of human interleukin-17A and interleukin-17F (IL-17A/F) or interferon-γ (IFN-γ) immunity are each associated with a specific set of infections. Inborn errors of IL-17A/F underlie chronic mucocutaneous candidiasis (CMC), which is characterized by infections of the skin, nails, and oral and genital mucosae with Candida albicans, typically in the absence of other infections. Five genetic etiologies of CMC have been reported, with mutations in five genes (1, 2). Inborn errors of IFN-γ underlie Mendelian susceptibility to mycobacterial disease (MSMD), which is characterized by selective susceptibility to weakly pathogenic mycobacteria, such as Mycobacterium bovis Bacille Calmette-Guérin (BCG) vaccines and environmental mycobacteria. Eighteen genetic etiologies of MSMD have been reported, involving mutations of nine genes (3, 4). Only a few patients display both candidiasis and mycobacteriosis, including some
patients with IL-12p40 and IL-12Rβ1 deficiencies, which impair IFN-γ immunity in all patients and IL-17A/F immunity in some patients (4). We studied seven patients from three unrelated consanguineous families with this unusual combination of infectious diseases but no known genetic disorder. A Palestinian child (Fig. 1A, Kindred A, patient P1; see also supplementary text) died at the age of 6 years from disseminated BCG disease.

Two other children (P2 and P3) in Kindred A had similar clinical presentations but survived and are now 7 and 4 years old, respectively. A 6-year-old Chilean child (Fig. 1A, Kindred B, P4; see also supplementary text) had disseminated BCG infection at age 16 months. Finally, three siblings from Saudi Arabia (Fig. 1A, Kindred C, P5, P6, and P7; see also supplementary text), ages 9, 6, and 3 years, had mycobacterial diseases caused by BCG in two children and by M. tuberculosis in the third. Six of the seven patients also had mucocutaneous candidiasis of varying severity (table S1).

### Bi-allelic RORC Mutations

We combined whole-exome sequencing and genome-wide linkage (GWL) analysis to search for homozygous genetic lesions in the three probands (P1, P4, and P6) (fig. S1). We identified a homozygous C/T mutation in the RORC gene in P1, P2, and P3, resulting in a missense Ser38→Leu (S38L) substitution in the RORγ isoform or a S71L substitution in the RORγT isoform (Fig. 1, A and B, and fig. S2). In P4, we identified a homozygous RORC/γT mutation converting the Gln329 (Q329) residue of RORγT (or Q308 in RORγT) into a stop codon (Fig. 1, A and B, and fig. S2). In P5, P6, and P7, we identified a homozygous C/T mutation converting the G441 residue of RORγT (or Q420 in RORγT) into a stop codon (Fig. 1, A and B, and fig. S2).

In each kindred, all unaffected family members were either homozygous or homozygous for the wild-type (WT) allele (Fig. 1A and fig. S2). The familial segregation of these mutant RORC alleles was therefore consistent with an autosomal recessive (AR) pattern of inheritance. There were no other genes mutated in the three kindreds among the 173 genes on the 6.87-Mb interval linked with disease (maximum LOD score 6.35). The S17L mutation affects a strictly conserved residue of the DNA binding domain of RORγT (Fig. 1B) and is predicted to be damaging by multiple software algorithms (5). The Q308X and Q420X (X signifies a stop codon) nonsense mutations are predicted to result in truncated proteins lacking part of the ligand-binding domain (fig. S2). In total, the Q308X and Q420X alleles were not found in 1052 controls from 52 ethnic groups in the 1000 Genomes Project (ExAC), and dbSNP databases; in our own cohort, the Q308X allele is homozygous in one individual of the ExAC database, indicating that it is unique to these two families.

#### Broad immunological phenotype

Mouse RORγT is expressed in lymphoid tissue inducer (LIIT) cells, type 3 innate lymphoid cells (ILC3), type 1 natural killer T (NKT) cells, some γδ T cells, immature CD4+CD8αβ+ thymocytes, and IL-17A/F–producing CD4+ γδ T cells [T helper 17 (Th17) cell] (6–12). ILC3, type 1 NKT, and γδ T cells fail to develop in Rorc−/− mice, and CD4+CD8αβ+ thymocytes have a reduced life span (11, 14). Rorc−/− mice display clinical signs consistent with LTI deficiency, including absence of palpable axillary and cervical lymph nodes (despite visible tonsils), and had reduced thymus size (fig. 2A). As in Rorc−/− mice, ILC3 were barely detectable in the patients’ blood (fig. S6). In Rorc−/− mice, the short life span of CD4+CD8αβ+ thymocytes results in an inability to use the most 5′ segments of the T cell receptor (TCR) Vγ array (13), including those encoding the Vγ chains of mycol-associated invariant T (MAIT) cells and type 1 NKT cells (16). High-throughput sequencing of the Trg/TRG and Treg loci revealed that 5′ Vγ gene segment use had decreased, whereas Vδ and Vγ usage was normal in Rorc−/− T cell clonotypes (fig. S6). Further, these patients lacked TR4 clonotypes using Vγ5 and distal 3′ Jγ pairings (fig. S6). In total, Rorc−/− T cell clonotypes, the usage of Vγ9 was elevated (fig. S6), consistent with antigen-driven peripheral expansion of this subset, perhaps driven by mycobacteria (19). Abolished use of the Vγ segments TRAV7′ (encoding Vγ24) and TRAV1′ (encoding Vγ7) was confirmed by quantitative polymerase chain reaction.

#### Complete RORγ and RORγT Deficiency

In mice and humans, the RORγ and RORγT isoforms are generated by transcription from different start sites (6–10) (Fig. 1B). Both molecules are transcription factors, but they have different expression patterns in inbred mice: RORγ is ubiquitously expressed, whereas RORγT is restricted to leukocytes (10). RORγT plays an important role in T cell development and function in mice (11, 12). Animals lacking only RORγT apparently have the same immunological phenotype as those lacking both isoforms (10). We first assessed the effect of Rorc mutations by transiently expressing WT and mutant RORγT and RORγT in human embryonic kidney 293T (HEK293T) cells in the presence and absence of stimulation with phorbol 12-myristate 13-acetate (PMA) and ionomycin. We detected both the WT and STIL RORγT proteins at the expected molecular mass of 56 kDa (Fig. 1C). The Q308X and Q420X RORγT mutant proteins had molecular weights consistent with truncation at residues 308 and 420, respectively (Fig. 1C). Similar results were obtained upon expression of Rorc (fig. S3). We then performed an electrophoretic mobility shift assay (EMSA) to assess the ability of the mutant RORγT and RORγ isoforms to respectively bind to RORE-2 and RORE-1, the consensus binding sites in the promoter of IL17A (fig. S3).

The three mutations abolished DNA binding of RORγT to RORE-2 (Fig. 1C) and of RORγT to RORE-1 (fig. S3), but not by disrupting the nuclear localization of the protein (fig. S3). Each mutation resulted in the loss of IL17A promoter activation by RORγT (Fig. 1D) or RORγ (fig. S4).

Thus, each mutant allele was associated with a complete loss of function of the two encoded protein isoforms, identifying these patients as cases of human AR complete RORγ/RORγT deficiency (hereafter referred to as Rorc−/− deficiency).
and resulted in a lack of both CD161+Vα7.2+ MAIT cells and Vα24+Vβ11+ type 1 NKT cells (Fig. 2, B and C, and fig. S7). Some Vα7.2+ cells other than MAIT cells have recently been shown to recognize Mycobacterium-derived mycolyl lipids (20); they were also missing in RORC−/− patients. Nevertheless, RORC−/− patients displayed only mild CD4+ and CD8+ T cell lymphopenia, with normal B and NK cell counts (Fig. 2D and table S2). These patients did not, therefore, have T cell deficiency [also known as “combined immunodeficiency (CID)], consistent with their lack of broad infectious and autoimmune phenotypes (21). Finally, the frequencies of circulating γδ T cells were normal (table S2). Overall, these RORC−/− patients displayed the general immunological features characteristic of Rorc−/− mice (11, 12, 14, 22, 23). These studies also revealed that the development of MAIT and other Vα7.2+ T cells is critically dependent on RORγT, which had been predicted but not shown in mice. No infectious phenotype can be unambiguously assigned to any of these individual immunological anomalies.

**Abolished production of IL-17A/F**

Given the critical role of murine RORγT in generating IL-17A/F- and IL-22-producing lymphocytes [including ILC3, γδ T cells, and Tγδ cells (II, 13, 24)] and the finding that patients with compromised IL-17A/F immunity are susceptible to muco-cutaneous candidiasis (I), we assessed the development and function of IL-17A/F-producing lymphocytes in the patients. Circulating ILC3 were too few to assess their production of IL-17. CD3+ T cells from RORC−/− patients displayed a severe impairment in the production of IL-17A, IL-17F, and IL-22, at both the mRNA (fig. S8) and the protein level (Fig. 3A), after polyclonal stimulation. CD4+ γδ T cells are a major source of IL-17A/F (9). Memory (CD45RA−) CD4+ T cells from RORC−/− patients produced much less IL-17A, IL-17F, and IL-22 than WT and heterozygous controls (Fig. 3B).
In contrast, the memory CD4+ T cells from these patients produced large amounts of IL-4, IL-5, and IL-13 (Fig. 3E). IFN-γ was also reduced, but large amounts of IL-17A were secreted, serving as a control (Fig. 3E). Finally, *Herpesvirus saimiri*-transformed CD4+ T cells from RORC−/− patients showed abolished induction of IL17A and IL-22 in RORC−/− patients. As CMC-causing germline mutations have previously been identified in IL17F, IL17RA, IL17RC, and ACT1 (1, 2, 26), we conclude that impaired IL-17A/F immunity in RORC−/− patients accounts for their development of CMC. Human IL-17A/F-producing ILC3, γδ T cells, and αβ T cells, or any of their subsets, may individually or collectively confer protection against *Candida*.

**Selective defect in IFN-γ production**

We then investigated the cellular mechanism underlying the patients’ surprising susceptibility to mycobacteria. The patients did not display chronic granulomatous disease or severe CID, which can underlie BCG disease (4). The CD3+ T cells (including both γδ and αβ T cells) from RORC−/− patients produced IFN-γ normally, after the stimulation of whole blood or peripheral blood mononuclear cells (PBMCs) with PMA and ionomycin (Fig. S10). Likewise, total CD4+ T cells, memory (CD45RA−) CD4+ T cells, naïve CD4+ T cells cultured under Th1-polarizing conditions, and *Herpesvirus saimiri*-transformed T cells from

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**Fig. 2.** RORC−/− patients display abnormal thymus size and TCRα rearrangement in line with their mild T cell lymphopenia with a complete absence of MAIT and type 1 NKT cells. (A) Computed tomography (CT) scan of P4’s chest at the age of 16 months compared with a CT scan of a healthy control. P4’s scan reveals right lung infiltrate and thymic hypoplasia. (B and C) PBMCs from WT controls, heterozygous family members, or RORC−/− patients were analyzed for MAIT (B) and type 1 NKT (C) cell frequencies by flow cytometry. Each plot is representative of n = 3 experiments. (D) Cell counts were performed on fresh blood samples from heterozygous family members (n = 4) and RORC−/− patients (n = 3). Dotted lines indicate the normal ranges for each lymphocyte population per microliter of blood, based on the results for healthy individuals tested at the Necker Hospital for Sick Children (Paris, France).
the patients produced IFN-γ normally (fig. S10). Overall, and in contrast to the IL-17A/F defect, RORC/T deficiency does not impair IFN-γ secretion in conditions of polyclonal stimulation. We next assessed Mycobacterium-specific IFN-γ responses from whole blood (fig. 5A) or PBMCs (fig. 5B) of RORC−/− patients, heterozygous family members, and healthy controls. The patients’ cells produced very little IFN-γ in response to treatment with BCG plus IL-12 (fig. 5, A and B). This defect was as profound as that seen in patients with IL-12Rβ2 deficiency (27). The production of IL-12p40 by RORC−/− cells was normal (fig. S11). Impaired IFN-γ production may account for mycobacterial diseases in RORC−/− patients. This IFN-γ defect was not secondary to excessive IL-4, IL-5, or IL-13 production (fig. S11) or to the IL-17A/F defect (fig. S12). Many single-gene immunodeficiencies do not predispose to BCG disease despite impaired or abolished development or function of various αβ T cell subsets, including CD4+ T cells (28), CD8+ T cells (29), type 1 NKT cells (30, 31), and MAIT cells (32). Even rare patients deficient in total αβ T cell function [ZAP70−/− (32), TRAC−/− (33)] have not been reported to develop BCG disease. Whole blood or PBMCs from such patients responded normally to treatment with BCG plus IL-12, except for patients lacking all functional αβ T cells (fig. S12). As MAIT cells were shown to respond to mycobacteria (94), we purified these

Fig. 3. Cellular mechanisms of compromised IL-17 immunity and CMC in RORC−/− patients. (A) Whole blood from healthy WT donors, heterozygous family members, or RORC−/− patients was activated by PMA and ionomycin in the presence of brefeldin A, then assayed by intracellular flow cytometry for the production of IL-17A and IL-22. (B) Naive and memory CD4+ T cells from WT controls (n = 7), heterozygous family members (n = 2), and RORC−/− patients (n = 3) were cultured with T cell activation and expansion (TAE) beads, and the culture supernatants were then assessed for secretion of the cytokine indicated (37). (C) Cytokine production by in vitro-differentiated CD4+ T cells from control donors and RORC−/− patients. Naive (CD45RA+CCR7+) CD4+ T cells were purified from the PBMCs of WT controls (n = 6) or RORC−/− patients (n = 3), then cultured in the presence of TAE beads alone or TAE beads together with polarizing stimuli to induce the differentiation of T11- or T117-type cells (37). After 5 days, culture supernatants were assessed for the secretion of the cytokines indicated. (D) Sorted CCR6+ memory CD4+ T cells from WT controls, heterozygous family members, and RORC−/− patients were initially polyclonally stimulated to generate T cell libraries, then cultured with autologous irradiated B cells, with or without a 3-hour pulse with C. albicans lysate (5 μg/ml) (37). Proliferation was assessed by evaluating radiolabel incorporation on day 4 and is expressed as Δcpm values (cpm counts per minute) (37). Dotted lines represent the cutoff values. The frequencies of specific T cells using the Poisson distribution were 315/106, 631/106, and 874/106 in WT control, heterozygous family member, and RORC−/− patient, respectively. (E) Concentrations of the indicated cytokines were measured in the supernatants from positive cultures (Δcpm values above the cut-off value) from experiments performed as in (D) with cells from WT controls, heterozygous family members, and RORC−/− patients (n = 2 each). Number of wells: n = 45 to 64 for WT controls, n = 4 to 10 for heterozygous family members, and n = 14 to 23 for RORC−/− patients. *P < 0.05 versus WT controls; in two-tailed Mann-Whitney tests with Bonferroni correction. Error bars in (B), (C), and (E) indicate SEM.
cells from WT donor PBMCs and added them to PBMCs from RORC−/− patients before BCG stimulation. The lack of MAIT cells in RORC−/− patients did not account for their impaired IFN-γ production (fig. S13). Overall, the absence of type 1 NKT cells, CD8+ T cells, and the poor development of IL-17A/F T cells may contribute marginally to mycobacterial susceptibility but do not account for the low level of IFN-γ production by RORC−/− leukocytes stimulated with BCG and IL-12, and probably not for the patients' mycobacterial disease.

Impaired IFN-γ production by γδ T cells

We thus systematically characterized the consequences of leukocyte population depletions on BCG-dependent IFN-γ production by PBMCs in healthy controls. We found no overt IFN-γ defect as a consequence of depletion NK cells, CD14+ cells, or CD4+ or CD8+ T cells. Depletion of γδ T cells, γδ T cells, or both resulted in diminished IFN-γ production (fig. S14). To probe the kinetics of this phenotype, a similar experiment was repeated and supernatant was assessed at 6, 12, 18, 24, and 48 hours poststimulation (fig. S14). The effect of γδ T cell depletion was most apparent at 24 hours (fig. S14). We observed high expression of RORC isoform 2 mRNA in both γδ and γδ T cells of healthy donors (fig. S15), prompting further analyses of γδ T cell function. Flow cytometry analyses revealed that the TCRVβhigh γδ T cells from RORC−/− patients could not secrete IFN-γ in response to stimulation with PMA and ionomycin, unlike TCRVβhigh γδ T cells (fig. S15). TCRVβ2+ T cells have been reported as the predominant cells responsible for human BCG vaccination (19). RORC−/− patients had normal frequencies of TCR Vβ2+ cells, but these cells were unable to secrete IFN-γ when stimulated with PMA and ionomycin (fig. S15), suggesting a possible contribution of this γδ T cell subset defect to mycobacterial susceptibility in RORC−/− patients. Overall, RORC-γδ T cell deficiency diminishes the IFN-γ-producing capacity of γδ T cells, which normally produce this cytokine in response to Mycobacterium stimulation.

The patients’ CD4+CCR6+ αβ T cells produce low IFN-γ in response to BCG

Previous studies have demonstrated that the T-cell and RORC-T-expressing, IFN-γ and IL-17A/F-producing CCR6+CXCR3+ T1H1+ subset is strongly enriched for Mycobacterium-responsive CD4+ αβ T cells, unlike the CCR6+CCR4+ T1H17 cells that only express RORC-T and produce IL-17A/F and are enriched for Candida-responsive T cells (25). We therefore purified memory (CD45RA−) αβ T cell subsets (fig. S9) and assessed their proliferation and cytokine production in response to a pool of BCG peptides. CD4+CCR6+ αβ T cells from RORC−/− patients had a normal or high frequency of antigen-specific cells recognizing BCG peptides, as demonstrated by the induction of proliferation (Fig. 5C and fig. S16). However, although CD4+CCR6+ T cells from RORC−/− patients responded to mycobacterial antigens, they secreted much less IFN-γ than CD4+CCR6+ αβ T cells from normal donors (Fig. 5D). The normal proliferation and cytokine production of other CD4+ memory T cell subsets in response to Candida and Mycobacterium (fig. S17) and to irrelevant viral stimuli (fig. S18) indicate a selective RORC-T-dependent functional defect in Mycobacterium-specific CD4+CCR6+ αβ T cells. Although we did not purify and test T1H1+ cells, they were present in normal proportions in the patients (fig. S9), implying that they are functionally defective for IFN-γ production upon Mycobacterium stimulation. Collectively, these data suggest that mycobacterial diseases in RORC−/− patients may result from the poor production of IFN-γ by γδ T cells, CCR6+CXCR3+CD4+ αβ T1H1+ cells, or both in response to mycobacteria. IFN-γ treatment may therefore be beneficial for RORC−/− patients. This combined defect probably also accounts for mycobacterial disease in severe combined immunodeficient patients, as patients with various forms of CID are normally resistant to BCG (27, 33). Finally, the lack of MAIT and type 1 NKT cells, reduction in ILC3, and possibly the absence of other lymphocytes not analyzed using blood samples (e.g., LIIT) may aggravate the mycobacterial phenotype of RORC−/− patients.

Conclusion

Collectively, these data demonstrate that human RORC plays a surprising dual role in host defense. These findings are clinically, immunologically, and genetically robust, as they were consistent in seven patients from three ethnic groups, homozygous for three different RORC mutations that are loss-of-function for both isoforms. Although the two infectious phenotypes are purely recessive, some immunological phenotypes showed codominant or dominant inheritance. The mild T cell lymphopenia, small thymus, lack of palpable axillary and cervical lymph nodes, and absence of MAIT and type 1 NKT cells in RORC−/− patients were consistent with the phenotype of Rorc−/− mice (table S3). Likewise, impaired IL-17A/F immunity was predicted to account for impaired protection against Candida albicans (35), as Rorc is the master gene controlling T1H7 differentiation in inbred mice (11), and mutations affecting human IL-17A/F immunity underlie isolated CMC (1, 26, 36). The IL-17A/F defect therefore underlies CMC in RORC-T-deficient patients, probably but not necessarily because of T cells, as other cells can produce these cytokines in healthy individuals. We expected these patients to be susceptible to candidiasis, but their susceptibility to mycobacterial disease and its severity were unanticipated. This phenotype does not seem to be human-specific, as we also found that mice deficient for Rorc (14) are susceptible to mycobacterial infection (fig. S19). Our data conclusively demonstrate that human RORC plays an indispensable role in the induction of IFN-γ-dependent antimycobacterial systemic immunity. The mechanism underlying disease in these patients probably involves an impairment of the induction of IFN-γ production by γδ T cells, CCR6+CXCR3+CD4+ αβ T1H1+ cells, or both in response to mycobacteria. Other mechanisms may also be at work. Human RORC is essential not only for the development of IL-17A/F-producing lymphocytes protecting the mucocutaneous barriers against Candida but also for the activation of IFN-γ-producing T cells and for systemic protection against Mycobacterium.
Fig. 5. Cellular mechanisms of impaired IFN-γ immunity to Mycobacterium in RORC<sup>−/−</sup> patients. (A) Whole-blood samples from healthy controls (<i>n</i> = 23), heterozygous family members (<i>n</i> = 4), or RORC<sup>−/−</sup> patients (<i>n</i> = 4) were incubated for 48 hours under three different sets of activation conditions: (i) medium alone, (ii) live <i>M. bovis</i>-BCG (BCG) at a multiplicity of infection of 20 BCG cells per leukocyte, and (iii) BCG plus 20 ng/ml IL-12. The IFN-γ levels of culture supernatants were determined by enzyme-linked immunosorbent assay (ELISA). (B) Equal numbers of live PBMCs from healthy controls, WT family members, heterozygous family members, or RORC<sup>−/−</sup> patients were cultured in the presence of live BCG, BCG and IL-12, or PMA/ionomycin for 48 hours. IFN-γ concentration in the culture supernatant was assessed by ELISA. (C) Sorted CCR6<sup>+</sup> memory CD4<sup>+</sup> T cells were polyclonally stimulated with PHA in the presence of irradiated allogeneic feeder cells and IL-2 to generate T cell libraries, as in Fig. 3D. Library screening was performed 14 to 21 days after initial stimulation by culturing thoroughly washed T cells with autologous irradiated B cells, with or without a 3-hour pulse with <i>M. bovis</i>-BCG peptide pools. Proliferation was measured by radiolabel incorporation on day 4 and is expressed as Δcpm values. Each symbol illustrates one culture. Dotted lines represent the cutoff value. The frequencies of specific T cells were calculated using the Poisson distribution were 467/10<sup>3</sup>, 749/10<sup>3</sup>, and 875/10<sup>3</sup> in WT control, heterozygous family member, and RORC<sup>−/−</sup> patient, respectively. (D) The cytokines indicated were determined in the culture supernatants from wells with Δcpm values above the cutoff value. Number of wells: <i>n</i> = 45 to 64 for WT controls, <i>n</i> = 4 to 10 for heterozygous family members, and <i>n</i> = 14 to 23 for RORC<sup>−/−</sup> patients. *<i>P</i> < 0.05 versus WT controls; in two-tailed Mann-Whitney tests with Bonferroni correction. Error bars in (D) indicate SEM.

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37. Materials and methods are available as supplementary materials on Science Online.

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**Discovery of a Weyl fermion semimetal and topological Fermi arcs**

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A Weyl fermion is a new state of matter that hosts Weyl fermions as emergent quasiparticles and admits a topological classification that protects Fermi arc surface states on the boundary of a bulk sample. This unusual electronic structure has deep analogies with particle physics and leads to unique topological properties. We report the experimental discovery of a Weyl semimetal, tantalum arsenide (TaAs). Using photoemission spectroscopy, we directly observe Fermi arcs on the surface, as well as the Weyl fermion cones and Weyl nodes in the bulk of TaAs single crystals. We find that Fermi arcs terminate on the Weyl fermion nodes, consistent with their topological character. Our work opens the field for the experimental study of Weyl fermions in physics and materials science.

Weyl fermions have long been known in quantum field theory, but have not been observed as a fundamental particle in nature (1–3). Recently, it was understood that a Weyl fermion can emerge as a quasiparticle in certain crystals, Weyl fermion semimetals (2–22). Despite being a gapless metal, a Weyl semimetal is characterized by topological invariants, broadening the classification of topological phases of matter beyond insulators. Specifically, Weyl fermions at zero energy correspond to points of bulk band degeneracy, Weyl nodes, which are associated with a chiral charge that protects gapless surface states on the boundary of a bulk sample. These surface states take the form of Fermi arcs connecting the projection of bulk Weyl nodes in the surface Brillouin zone (BZ) (6). A band structure like the Fermi arc surface states would violate basic band theory in an isolated two-dimensional (2D) system and can only arise on the boundary of a 3D sample, providing a dramatic example of the bulk-boundary correspondence in a topological phase. In contrast to topological insulators where only the surface states are interesting (21, 22), a Weyl semimetal features unusual band structure in the bulk and on the surface. The Weyl fermions in the bulk are predicted to provide a condensed-matter realization of the chiral anomaly, giving rise to a negative magnetoresistance under parallel electric and magnetic fields, unusual optical conductivity, nonlocal transport, and local nonconservation of ordinary current (5, 12–16). At the same time, the Fermi arc surface states are predicted to show unconventional quantum oscillations in magneto-transport, as well as unusual quantum interference effects in tunneling spectroscopy (17–19). The prospect of the realization of these phenomena has inspired much experimental and theoretical work (1–22).

Here we report the experimental realization of a Weyl semimetal in a single crystalline material, tantalum arsenide (TaAs). Using the combination of the vacuum ultraviolet (low-photon-energy) and soft x-ray (SX) angle-resolved photoemission spectroscopy (ARPES), we systematically and differentially study the surface and bulk electronic structure of TaAs. Our ultraviolet (low-photon-energy) ARPES measurements, which are highly surface sensitive, demonstrate the existence of the Fermi arc surface states, consistent with our band calculations presented here. Moreover, our SX-ARPES measurements, which are reasonably bulk sensitive, reveal the 3D linearly dispersive bulk Weyl cones and Weyl nodes. Furthermore, by combining the low-photon-energy and SX-ARPES data, we show that the locations of the projected bulk Weyl nodes correspond to the terminations of the Fermi arcs within our experimental resolution. These systematic measurements demonstrate TaAs as a Weyl semimetal.

The material system and theoretical considerations

Tantalum arsenide is a semimetallic material that crystallizes in a body-centered tetragonal lattice system (Fig. 1A) (23). The lattice constants are a = 3.437 Å and c = 11.656 Å, and the space group is I4₁md (*140), as consistently reported in previous structural studies (23–25). The crystal consists of interpenetrating Ta and As sublattices, where the two sublattices are shifted by (1/4, 1/4, 1/2). The diffraction data match well with the lattice parameters and the space group I4₁md (26). The scanning tunneling microscopic (STM) topography (Fig. 1B) clearly resolves the (001) square lattice without any obvious defect. From the topography, we obtain a lattice constant a = 3.45 Å. Electrical transport measurements on TaAs confirmed its semimetallic transport properties and reported negative magnetoresistance, suggesting the anomalies due to Weyl fermions (25).

Discussion

We discuss the essential aspects of the theoretically calculated bulk band structure (9, 10) that predicts TaAs as a Weyl semimetal candidate. Without spin-orbit coupling, calculations (9, 10) show that the conduction and valence bands interpenetrate (dip into) each other to form four 1D line nodes (closed loops) located on the k_x and k_y planes (shaded blue in Fig. 1, C and E). Upon the inclusion of spin-orbit coupling, each line node loop is gapped out and shrinks into six Weyl nodes that are away from the k_x = 0 and k_y = 0 mirror planes (Fig. 1E, small filled circles). In our calculation, in total there are 24 bulk Weyl cones (9, 10), all of which are linearly dispersive and are associated...