Many enzymes use nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP), collectively referred to as NAD(P), as essential coenzymes. These enzymes often do not share significant sequence identity and cannot be easily detected by sequence homology. Previously, we determined all distinct locally conserved pyrophosphate-binding structures (3d motifs) from NAD(P)-bound protein structures, from which 1d sequence motifs were derived. Here, we aim to establish the precision of these 3d and 1d motifs to annotate NAD(P)-binding proteins. We show that the pyrophosphate-binding 3d motifs are characteristic of NAD(P)-binding proteins, as they are rarely found in non-NAD(P)-binding proteins. Furthermore, several 1d motifs could distinguish between proteins that bind only NAD and those that bind only NADP. They could also distinguish between NAD(P)-binding proteins from non-NAD(P)-binding ones. Interestingly, one of the pyrophosphate-binding 3d and corresponding 1d motifs was found only in enoyl-acyl carrier protein reductases, which are enzymes essential for bacterial fatty acid biosynthesis. This unique 3d motif serves as an attractive novel drug target, as it is conserved across many bacterial species and is not found in human proteins.
Figure 1 | Derivation of 1d-motifs from distinct 3d-motifs. (Left) The distinct locally conserved pyrophosphate-binding \( \beta \alpha \) structures derived from NAD(P)-binding domains where the total number of \( \beta \alpha \) structures exceeds 25. The \( \beta \alpha \) structure is in green with the regions containing conserved glycines highlighted in yellow, while NAD(P) is shown in stick format. The class III and IV structures share a common backbone conformation but exhibit different side chain orientations: in the class IV structure (1zk4-A), the Leu side chain is shown in stick, but the corresponding side chain in the class III structure (1sby-A), indicated by the black arrow, point in an opposite direction. (Right) Sequence logos derived from aligning the same-length sequences comprising the distinct pyrophosphate-binding \( \beta \alpha \) structures and corresponding 1d motif. Glycine is shown in green, polar (S, T, Y, N, Q, H, K, R, D, E) residues in blue, and nonpolar (A, V, L, I, P, W, F, C, M) residues in black.
structures, labeled I, ..., XII, are present in nearly three-quarters of the NAD(P)-binding domains in the Protein Data Bank (PDB)\textsuperscript{16}. Sequence motifs were then derived from class I, II, III, IV, and XII structures, but not from the other 3d motifs, which do not have enough sequences (\(\leq 14\)) to generate statistically significant 1d motifs. The same-length sequences from NAD and NADP-bound structures comprising each pyrophosphate-binding structural class in Fig. 1 were aligned separately. For example, out of 105 structures with the class IV 3d motif, 45 contain NAD and 60 contain NADP; alignment of the 45 sequences from the NAD-bound structures with the class IV 3d motif yielded [AVI]-[LVIFA]-[IV]-T-G-[GAS]-X\(_2\)-G-X-G-X\(_T\)-[LFA], whereas alignment of the 60 sequences from the NADP-bound structures comprising the same 3d motif yielded [AVIC]-[LVIV]-[VIL]-T-G-[AGSC]-X\(_2\)-[GR]-[ILF]-G-X\(_T\)-[LLF]. The consensus NAD(P)-binding sequences derived from the 3d motifs in Fig. 1 appear to be statistically significant, as they are found in \(\leq 1.2\%\) of randomized sequences (see Supplementary Table S1), except for the NADP-binding consensus sequences corresponding to structural class III (\(\sim 3.6\%\)) and class I (14\%)\textsuperscript{16}. However, the randomized sequences are not real biological sequences, therefore the potential of these NAD(P) 1d motifs to annotate NAD(P)-binding proteins remains unclear.

In this work, we address the following questions: (1) How often do the distinct pyrophosphate-binding 3d motifs in Fig. 1 occur in nonNAD(P)-binding proteins? (2) Since the 1d motifs in Fig. 1 were derived from either NAD or NADP-bound proteins, can they distinguish between proteins that bind only NAD and those that bind only NADP? (3) Can the NAD(P) pyrophosphate-binding 1d motifs distinguish between NAD(P)-binding proteins and nonNAD(P)-binding ones? In particular, can they differentiate proteins that bind FAD, which is similar to NAD and also has a pyrophosphate group? Notably, we are interested in the precision (fraction of correctly predicted NAD(P)-binding proteins) of the motifs in Fig. 1. To address these questions, we created four datasets of 3d structures and seven datasets of 1d sequences (see Table 1). The results show that the 3d motifs in Fig. 1 are statistically significant, as they are rarely found in 3d structures of nonNAD(P)-binding proteins. Several 1d motifs could correctly distinguish between proteins that bind only NAD and those that bind only NADP. Furthermore, 1d motifs derived from class II, IV, and XII 3d motifs can be used to distinguish NAD(P)-binding proteins from nonNAD(P)-binding ones.

### Results

#### Four pyrophosphate-binding 3d motifs are characteristic of NAD(P)-binding proteins.

To assess if the distinct pyrophosphate-binding 3d motifs in Fig. 1 are characteristic of NAD(P)-binding proteins, we computed the occurrence frequency of a 3d motif corresponding to structural class j in \(\leq 3.5\) Å protein structures containing (1) NAD(P), (2) FAD, (3) phosphate-containing ligands including FAD, and (4) no NAD(P), FAD, or phosphate groups. For each of these 3d motifs, the percentage occurrence frequency in the NAD(P)-binding proteins is significantly greater than that in the NADP(P)-free proteins, except the class I 3d motif, which appears more often in FAD-binding proteins than in NAD(P)-binding ones (see Table 2). All the pyrophosphate-binding 3d motifs except the class I motif can distinguish NAD(P)-binding proteins from nonNAD(P)-binding proteins with positive predictive values (PPVs) \(\geq 83\%). Interestingly, the class IV and XII 3d motifs seem to be unique to NAD(P)-binding proteins, as they were not found in any of the NADP(P)-free structures. The class III 3d motif, which has a similar backbone structure as the class IV motif but different side chain orientations (see Fig. 1), is not found in any of the FAD structures and rarely in the other NAD(P)-free structures (PPV \(\sim 92\%\)). The class I 3d motif, which occurs most frequently in NAD(P)-binding proteins, can differentiate NAD(P)-binding proteins from nonphosphate-binding ones (PPV \(\sim 80\%\)), but not from proteins that bind phosphate-containing ligands (PPV \(\sim 51\%\)).

#### Four pyrophosphate-binding 1d motifs can distinguish between NAD- and NADP binding proteins.

Some of the 3d motifs in Fig. 1 appear to be NAD or NADP-specific; e.g., the class II 3d motif was found only in NADP-bound structures, while the class XII 3d motif was found predominantly in NAD-bound structures. Furthermore, the pyrophosphate-binding 1d motifs were derived from NAD and NADP-bound protein structures separately\textsuperscript{16} (see Fig. 1). To determine if the pyrophosphate-binding 1d motifs can distinguish between NAD- and NADP-binding proteins, the % occurrence frequencies of the 1d motifs in the 1d-NAD and 1d-NADP datasets and PPVs were computed (see Table 3). Four of the 1d motifs can distinguish between NAD and NADP-binding proteins with PPVs \(\geq 76\%). Remarkably, the II_NADP motif derived from class II NADP-bound protein structures was not found in any of the NAD-binding proteins, whereas the XII_NAD motif derived from class XII NAD-bound protein structures was not found in the 1d-NADP dataset.

### Table 1: Description of data sets employed

| Redundant Dataset | Description of dataset |
|-------------------|------------------------|
| 3d-NAD(P)         | Protein structures with NAD(P) bound |
| 3d-FAD            | Protein structures with FAD bound |
| 3d-PO4            | Protein structures with \(\geq 1\) phosphate group bound, excluding NAD(P) but including FAD |
| 3d-nonPO4         | Protein structures with no bound NAD(P) or phosphate |
| 1d-NAD(P)         | Sequences of NAD(P)-binding proteins |
| 1d-NAD            | Sequences of proteins that bind only NAD |
| 1d-NADP           | Sequences of proteins that bind only NADP |
| 1d-nonNAD(P)      | Sequences of nonNAD(P)-binding proteins |
| 1d-FAD            | Sequences of FAD-binding proteins |
| 1d-PO4            | Sequences in 1d-NAD(P) that bind \(\geq 1\) phosphate, including FAD-binding protein sequences |
| 1d-nonPO4         | Sequences in 1d-NAD(P) that do not bind phosphate |

### Table 2: Frequency distribution of the NAD(P) pyrophosphate-binding 3d motifs in the PDB

| Class j | NAD(P) | FAD | PO4 | nonPO4 | NAD(P) vs. FAD | NAD(P) vs. PO4 | NAD(P) vs. nonPO4 | NAD(P) vs. PO4 |
|---------|-------|-----|-----|-------|---------------|---------------|-----------------|---------------|
| I       | 24.6  | 36.2| 2.6 | 0.2   | 68            | 51            | 80              | 51            |
| II      | 2.2   | 0.3 | 0.05| 0.01  | 96            | 83            | 89              | 83            |
| III     | 12.9  | 0   | 0.1 | 0.04  | 100           | 92            | 92              | 92            |
| IV      | 11.3  | 0   | 0   | 0     | 100           | 100           | 100             | 100           |
| XII     | 1.6   | 0   | 0   | 0     | 100           | 100           | 100             | 100           |

*The number of structures in the given dataset containing the 3d motif belonging to class j divided by the total number of structures/proteins in the given dataset, multiplied by 100.

\[\text{Table 1} | \text{Description of data sets employed}
\[\text{Table 2} | \text{Frequency distribution of the NAD(P) pyrophosphate-binding 3d motifs in the PDB}
\]
Interestingly, dataset, which contains sequences from the UniProtKB/Swiss-Prot answer this question, the 1d motifs were tested on the 1d-FAD motifs in Fig. 1 also bind the FAD pyrophosphate group? To binding proteins 1d motifs can distinguish between NAD(P)-binding and FAD-3d motif that bind only NADP. The difference in specificity of the second conserved glycine followed by hydrophobic resi-IV_NADP motifs indicates that the allowance of arginine at the posi-
tion of the second conserved glycine followed by hydrophobic resi-
dues; i.e., [GR]-[ILF], seems to be a signature of proteins with class IV

1d motifs can distinguish between NAD(P)-binding and FAD-
binding proteins. Since FAD is most similar to NAD, do the 1d motifs in Fig. 1 also bind the FAD pyrophosphate group? To answer this question, the 1d motifs were tested in the 1d-FAD dataset, which contains sequences from the UniProtKB/Swiss-Prot June 2013 database^1. Interestingly, although the pyrophosphate group is common to both FAD and NAD(P), the 1d motifs in Fig. 1 appear to recognize specifically the NAD(P) pyrophosphate with PPVs ≥ 96%, except for the 1d_NAD motif where the PPV is 84%. Notably, the 1d motifs derived from the class II, IV, and XII 3d motifs were not found in the 1d-FAD dataset.

1d motifs derived from class II, IV, and XII 3d motifs can distinguish between NAD(P)- and nonNAD(P)-binding proteins. To determine if the 1d motifs derived from NAD(P)-bound protein structures can distinguish between NAD(P) and nonNAD(P)-binding proteins, the % occurrence frequencies of the 1d motifs in the 1d-NAD(P), 1d-PO4 (which include FAD-binding sequences), 1d-nonPO4, and 1d-nonNAD(P) datasets were computed. Sequences in the 1d-PO4 and 1d-nonPO4 datasets comprise the 1d-nonNAD(P) dataset. The results in Table 4 show that although the number of NAD(P)-binding proteins is an order of magnitude less than the number of nonNAD(P)-binding proteins, the % occurrence frequencies of the 1d motifs in the 1d-NAD(P) dataset are significantly greater than those in the 1d-PO4 or 1d-
nonPO4 dataset. Like the class IV and XII 3d motifs, the IV_NAD, IV_NADP, and XII_NAD motifs seem to be unique to NAD(P)-

 Ing. 3d and 1d motifs in human proteome annotation. All the 3d motifs in Fig. 1 (except class I), which could distinguish between NAD(P)- and nonphosphate-binding proteins with ≥90% PPV (see Table 2) were used to predict NAD(P)-binding proteins in human structures from the June 2013 release of the PDB^6. Interestingly, the class XII 3d motif was not found in any human protein structure. The class II, III and IV 3d motifs were found in 41 human proteins, whose structures indeed contain NAD(P), confirming all the predictions.

The 1d motifs derived from the class IV and XII 3d motifs, which could distinguish between NAD(P)- and nonNAD(P)-binding proteins with 100% PPV (see Table 4), were used to predict NAD(P)-

binding proteins in human sequences from the June 2013 UniProtKB/Swiss-Prot database^1. Like the class XII 3d motif, the XII_NAD motif was not found in any human protein sequence

Table 3 | Precision of the 1d motifs to distinguish between NAD- and NADP-binding proteins

| 1d motif | Consensus sequence | NAD^a | NAD^a | %PPV |
|----------|-------------------|-------|-------|-------|
| I_NAD    | [VLCAF]X2-GX2-GX2-[IVAMLF]GX2-[AIKYFVMW] | 18.5  | 6.5   | 82^b  |
| I_NADP   | [VLIF]X2-GX2-[GSA]X2-[GAS]X2-[LAIFWCG] | 9.3   | 22.6  | 61^b  |
| II_NADP  | [IVL][IX][IVC]X2-GX2-[VIL]YY2-[AFMCLV]-[LMIVF] | 0     | 0.4   | 100^c |
| III_NAD  | [VIFW]X2-VLIFX2-GX2-[AGC]X2-[IFL]-[IYAFV] | 2.4   | 7.5   | 34^c  |
| III_NADP | [VIFL]X2-VLIFX2-[GA]X2-GX2-[ ILF] | 2.8   | 3.9   | 47^c  |
| IV_NAD   | [AVI][IVFA]-[IV]X2-[GAS]X2-GX2-[ILF] | 0.5   | 2.3   | 26^c  |
| IV_NADP  | [AVIC][IVF]-[IV]X2-[AGSC]X2-[GR]-[ILF]-[IFL]-[FY]X2-X2-A | 0.4   | 1.8   | 76^c  |
| XII_NAD  | [LVIF]X2-VLIFX2-[SAG]X2-[AG]-[WIFY]X2-[IV]A | 0.06  | 0     | 100^b |

^aThe number of protein sequences in the given dataset matching the 1d motif divided by the total number of sequences in the given dataset, multiplied by 100.

^bThe number of true positives is the number of NADP-binding sequences matching a 1d motif derived from NADP-bound structures, whereas the number of false positives is the number of NADP-binding sequences matching the same 1d motif.

^cThe number of false positives is the number of NADP-binding sequences matching a 1d motif derived from NADP-bound structures, whereas the number of false positives is the number of NADP-binding sequences matching the same 1d motif.

Table 4 | Precision of the 1d motifs to distinguish between NAD(P)-binding and nonNAD(P)-binding proteins

| 1d motif | % frequency of 1d motif in 1d dataset^a | % PPV of 1d-NAD(P) vs. |
|----------|----------------------------------------|-------------------------|
| I_NAD    | 13.2                                   | 96%                     |
| I_NADP   | 12.4                                   | 78%                     |
| II_NADP  | 0.1                                   | 100%                    |
| III_NAD  | 4.8                                   | 99%                     |
| III_NADP | 3.1                                   | 97%                     |
| IV_NAD   | 1.2                                   | 100%                    |
| IV_NADP  | 1.0                                   | 100%                    |
| XII_NAD  | 0.07                                  | 100%                    |

^aThe number of protein sequences in the given dataset matching the 1d motif divided by the total number of sequences in the given dataset, multiplied by 100.
The IV_NAD and IV_NADP motifs predicted 25 and 21 NAD(P)-binding proteins, respectively, out of which two are novel (accession numbers Q8N5I4 and Q96LJ7). The II_NADP 1d motif, which can discern NAD(P)-binding proteins from nonphosphate-binding ones with 100% PPV, predicted two NAD(P)-binding human sequences, one of which is novel (accession number Q9GZT4).

Discussion

This work has shown that the distinct locally conserved structures employed by NAD(P)-binding proteins for the same function; viz., binding the pyrophosphate, rarely occur in other proteins, especially those do not bind phosphate-containing ligands. Given a novel structure of a protein with unknown function, the 3d motifs in Fig. 1 could help to not only identify a NAD(P)-binding protein, but also suggest the pyrophosphate-binding site. This could in turn help to dock the cofactor to the protein. Given a novel sequence with little homology to existing sequences, 1d motifs derived from class IV and XII 3d motifs, which are not found in any nonNAD(P)-binding proteins, can be used to annotate NAD(P)-binding proteins, whereas the II_NADP motif, which was not found in nonphosphate-binding proteins, can distinguish between NAD(P)- and nonphosphate-binding proteins. These 1d motifs predicted three novel NAD(P)-binding human sequences.

This work has also shown the usefulness of the motifs by revealing a novel drug target region with unique sequence and structural characteristics: The locally conserved class XII phosphate-binding structure and sequence are found only in bacterial enoyl-acyl carrier protein reductases (EC 1.3.1.9/1.3.1.10), which are key enzymes of the type II fatty acid synthesis system. Because new antibiotics are urgently needed for multidrug-resistant bacteria and the function of enoyl-acyl carrier protein reductase is essential for the bacterial survival17, the class XII 3d motif serves as an attractive novel drug target region since it is conserved across many bacterial species and is not found in any human proteins.

Methods

Dataset of NAD(P)-bound protein structures. A set of redundant NAD(P)-binding protein structures was created by searching the June 2013 release of the PDB for ≤3.5 Å X-ray structures of proteins bound to oxidized or reduced NAD(P). If a NAD(P)-binding protein has multiple structures, then the highest resolution structure was chosen. If the structure contains multiple subunits, only one representative conformation was included. This generated 1,096 NAD(P)-binding proteins in the 3d-NAD(P) dataset (Fig. 2, left).
Datasets of NAD(P)-binding sequences. All NAD(P)-binding sequences were extracted from the manually curated UniProtKB/Swiss-Prot June 2013 database¹ by searching for the ligand keyword NAD or NADP. They were compared to those in the PDB and identical sequences were removed. This yielded a set of 24,516 NAD(P)-binding sequences (1d-NAD(P) dataset). To create a set of protein sequences that bind only NAD (1d-NAD) and another set of sequences that bind only NADP (1d-NADP), the annotated NAD-binding and NADP-binding sequences in the 1d-NAD(P) dataset were compared. Those sharing ≥40% sequence identity were removed, as such sequences may bind both NAD and NADP. This yielded 15,340 NAD-binding and 6,722 NADP-binding sequences (Fig. 2, right).

Dataset of NAD(P)-free protein structures. To obtain NAD(P)-free protein structures, the sequences of all proteins with ≤3.5 Å PDB structures were compared with the NAD(P)-binding sequences using CD-HIT-2D¹⁸. Those sharing ≥40% sequence identity were removed, as these structures might be similar to the NAD(P)-bound protein structures so their sequences might bind NAD(P). Sequences predicted by PSI-BLAST¹⁹ to be NAD(P)-binding with an E-value < 0.005 were also removed. The remaining NAD(P)-free protein structures were divided into two groups: (i) those containing nucleic acids or cofactors with phosphate groups and (ii) those without any bound phosphate. The first group contained 10,292 NAD(P)-free structures with phosphate groups and the second group comprised 33,514 NAD(P)-free structures with no phosphate groups (3d-PO⁴ dataset) (Fig. 2, left). From the 3d-PO⁴ dataset, 348 structures that contained FAD were extracted to generate the 3d-FAD dataset.

Secondary structure prediction. To determine whether a PDB structure contained any of the distinct pyrophosphate-binding 3d motifs in Fig. 1, we used two similarity measures: (1) the root-mean-square deviation of Cα atoms (RMSDα) and (2) the root-mean-square deviation of dihedral angles (RMSDφ). First, a 12-residue sliding window was used to scan each protein in the 3d structures (see above). Each 12-residue segment, described by a vector of backbone φ and ψ dihedral angles V{φ₁,ψ₁,…,φ₁₂,ψ₁₂}, was superimposed upon the central 12 residues of each distinct pyrophosphate-binding structure, described by the vector V{φ₁₂,ψ₁₂,…,φ₁,ψ₁}. The RMSDα was computed according to:

$$\text{RMSD}_\alpha(V_1, V_2) = \sqrt{\sum_{i=1}^{12} (\phi_i(V_1) - \phi_i(V_2))^2 + (\psi_i(V_1) - \psi_i(V_2))^2}/22 \quad (1)$$

The PDB structure containing V{φ₁₂,ψ₁₂,…,φ₁,ψ₁}, was considered to possess a given pyrophosphate-binding structure in Fig. 1 if the RMSDα was ≤3.0 Å and the pairwise Cα RMSD was ≤1.0 Å (Fig. 3, left).

1. Magrane, M. & the, Uniprot & Consortium. UniProt Knowledgebase: a hub of integrated protein data. Database 2011, bar009 (2011).
2. Yates, S. P., Jorgensen, R., Andersen, G. & Merrill, A. R. Stealth and mimicry by deadly bacterial toxins. Trends Biochem. Sci. 31, 123–133 (2006).
3. Peralta-Leal, A. et al. PARP inhibitors: New partners in the therapy of cancer and inflammatory diseases. Free Radic. Biol. Med. 47, 13–26 (2009).
4. Kirkland, J. B. Poly ADP-ribose polymerase-1 and health. Exp. Biol. Med. 235, 561–568 (2010).
5. Watson, J. D., Laskowski, R. A. & Thornton, J. M. Predicting protein function from sequence and structural data. Curr. Opin. Struct. Biol. 15, 275–284 (2005).
6. Sigrist, C. J. et al. PROSITE: a documented database using patterns and profiles as motif descriptors. Brief. Bioinform. 3, 265–274 (2002).

7. Mathura, V. S., Schein, C. H. & Braun, W. Identifying property based sequence motifs in protein families and superfamilies: application to DNase-I related endonucleases. Proteins 19, 1381–1390 (2003).

8. Hulo, N. et al. The PROSITE database. Nucleic Acids Res. 34, D227–D230 (2006).

9. Wass, M. N. & Sternberg, M. J. E. ConFunc—functional annotation in the twilight zone Bioinformatics 24, 798–806 (2008).

10. Wu, C. Y., Chen, Y. C. & Lim, C. A structural-alphabet-based strategy for finding structural motifs across protein families. Nucleic Acids Res., 38, e150 (2010).

11. Wu, C. Y., Hwa, Y.-H., Chen, Y. C. & Lim, C. Hidden Relationship between conserved residues and locally conserved phosphate-binding structures in NAD(P)-binding Proteins. J. Phys. Chem. B 116, 5644–5652 (2012).

12. Rossmann, M. G., Liljas, A., Branden, C. I. & Banaszak, L. T. Evolutionary and structural relationships among dehydrogenases. The Enzymes 11, 61–102 (1975).

13. Bellamacina, C. R. The nicotinamide dinucleotide binding motif: a comparison of nucleotide binding proteins. Faseb J. 10, 1257–1269 (1996).

14. Kleger, G. & Eisenberg, D. GXGGX and GXXXA Motifs Stabilize FAD and NAD(P)-binding Rossmann Folds Through Cx=HO Hydrogen Bonds and van der Waals Interactions. J. Mol. Biol. 323, 69–76 (2002).

15. Brakoulias, A. & Jackson, R. M. Towards a structural classification of phosphate binding sites in protein-nucleotide complexes: An automated all-against-all structural comparison using geometric matching. Proteins. 56, 250–260 (2004).

16. Berman, H. M. et al. The Protein Data Bank. Acta Crystallogr. Sect. D Biol. Crystallogr. 58, 899–907 (2002).

17. Lu, X., Huang, K. & You, Q. Enoyl acyl carrier protein reductase inhibitors: a patent review (2006–2010). Expert Opin. Ther. Patents 21, 1007–1022 (2011).

18. Li, W. & Godzik, A. Cd-hit: a fast program for clustering and comparing large sets of protein or nucleotide sequences. Bioinformatics 22, 1658–1659 (2006).

19. Altschul, S. F. et al. Gapped BLAST and PSI-BLAST: A new generation of protein database search programs. Nucleic Acids Res. 25, 3389–3402 (1997).

20. Mirabello, C. & Pollastr, G. Porter, PaleAle 4.0: high-accuracy prediction of protein secondary structure and relative solvent accessibility. Bioinformatics 29, 2056–2058 (2013).

21. Sievers, F. et al. Fast, scalable generation of high-quality protein multiple sequence alignments using Clustal Omega. Mol. Syst. Biol. 7, 539 (2011).

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Author contributions
Y.H.H. and C.Y.W. performed the research. K.S. helped with statistical analyses. Y.H.H. prepared figure and tables. C.L. designed the project and wrote the manuscript text. All authors reviewed the manuscript.

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