Key (Tooth)

Upper Right   Upper Left

52 51 61 62
53   63
54   64
First molar
55   65
Second molar

85   75
84   74
83   73
82 81 71 72

Lower Right   Lower Left

Single-tooth status

- ● ConfidentH (H)
- ● RelativeH (RH)
- ● Caries (C)

Metagenomics analyzed

No   Yes

A

Cohort A (N=637)
Cohort B (N=1867)
Children cohorts

16S rRNA amplicon sequencing for 2504 samples

Shotgun whole metagenomic sequencing (WGS) for 24 samples

Taxonomic abundance

- ■ Samples w/ 16S data
- ■ Samples w/ paired 16S and WGS data
- ■ Samples w/ predicted WGS data

N=2504

Functional abundance

N=24

Meta-Apo

Predictive functional abundance

N=2504

Key (Host)

Host group	T1	T2	Tn
H2H (stay healthy group)	●	●	●
H2C (caries-onset group)	●	●	●
C2C (caries-progression group)	●	●	●

B Spatial discovery cohort (Cohort A: 20 teeth/child)

Time of sample collection

H2H   C2C   T1   T2

2 visits
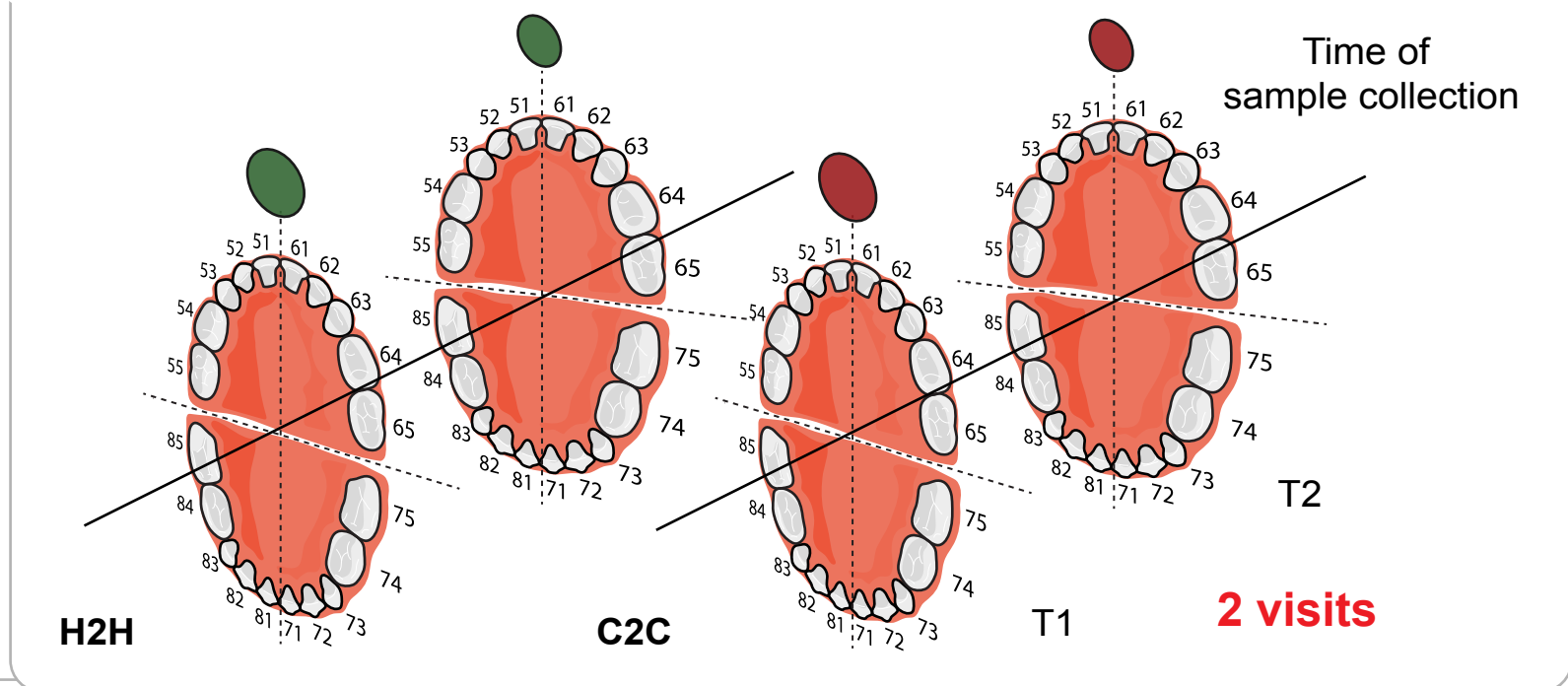
C Spatio-temporal discovery cohort (Cohort B: 9 teeth/child)

Time of sample collection

H2H   H2C   C2C   T5

T2,T3,T4   **5 visits**

T1
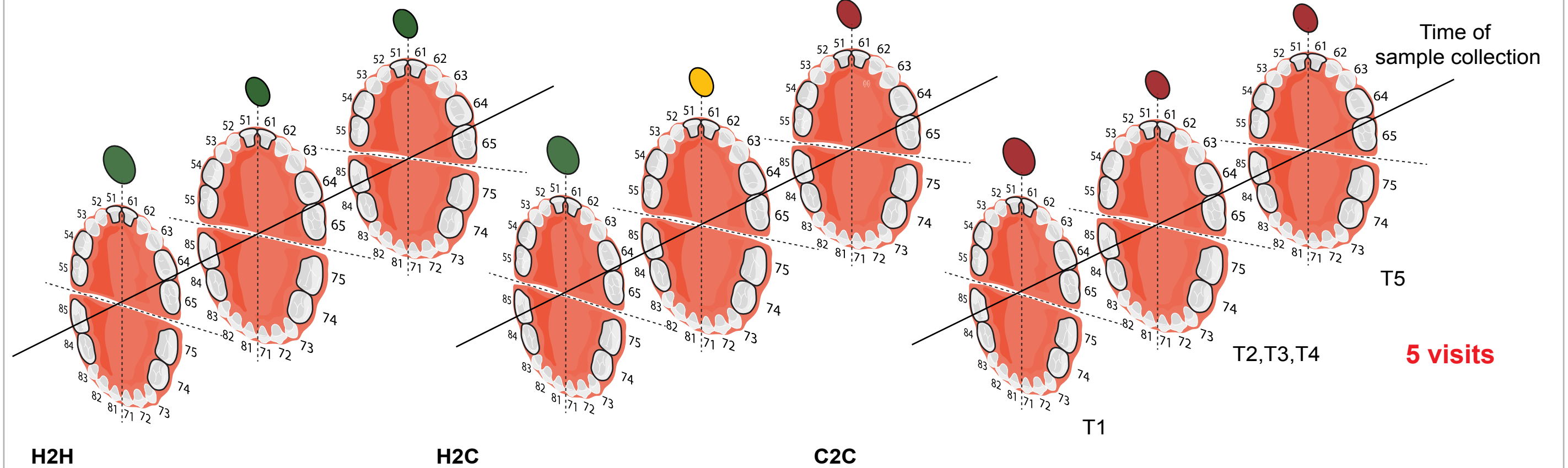
D

	Sample size	Population size	Number of teeth analyzed	Tooth numbers analyzed	Number of time points of sample collection	Metagenomics method used
Cohort A	637	16	20	[55, 54, 53, 52, 51, 61, 62, 63, 64, 65, 85, 84, 83, 82, 81, 71, 72, 73, 74, 75]	2	16S rRNA sequencing (N = 637 + 1867 = 2504) + WGS (N = 24) -> KEGG functional prediction (N = 2504)
Cohort B	1867	73	9	[55, 54, 51/61, 64, 65, 85, 84, 74, 75]	5	