Supplemental figures

Supplemental figures.

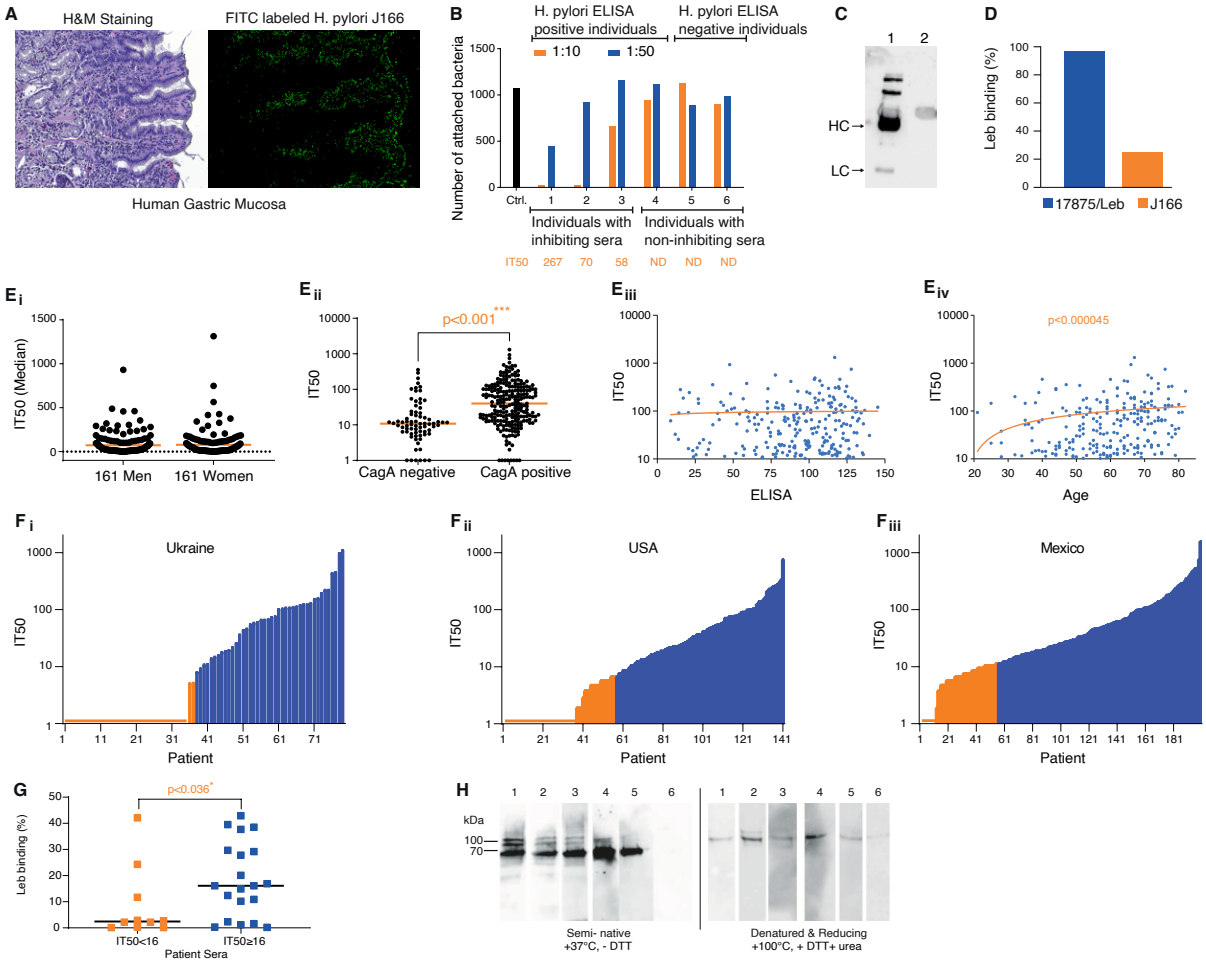


Figure S1. High global prevalence of serum inhibition of Leb binding

(**A***i*) H&E-stained adjacent sections of human gastric mucosa from Figure 1A, (A*ii*) and *in vitro* attachment by *H. pylori* J166 bacterial cells labeled with FITC-green fluorescence.

(**B**) Quantification by ImageJ of attached J166 bacteria treated with 1:10 and 1:50 dilutions of individual serum samples from **Figure 1A**. Individuals 1-4 were ELISA positive for *H. pylori* infection, whereas individuals 5 and 6 were ELISA negative. Individuals 1–3 demonstrated IT50s of 267, 70, and 58, in contrast to individuals 4–6 with non-detectable (ND) titers (**Figure 1B**).

(**C**) Immunoblot of the SDS-PAGE-separated serum proteins from individual 1 (from **Figure 1A**) detected with anti-human Ab. The heavy chain (HC) and light chain (LC), i.e., the IgG components, were fully removed by Protein G affinity desorption (sera before (1) and after (2) IgG desorption).

(**D**) *H. pylori* J166 with only 25% “Hot-Leb binding” is a low-affinity Leb-binding strain, compared to 17875/Leb, with >95% “Hot-Leb binding” which is a high-affinity Leb binding strain. High and low-affinity Leb-binding *H. pylori* strains have been identified (**Figure S2B**). The 25% Hot-Leb binding by strain J166 corresponds to ~50-fold lower affinity

according to Scatchard tests, which is a radio immuno-assay (RIA) for affinity testing based on binding of Leb under equilibrium conditions [42].

(**E***i*) Among the 322 Kalixanda Swedish *H. pylori* carriers (95% of whom were gastric healthy), the 161 men with median age 59 years and 161 women with median age of 61 years did not exhibit any difference in median IT50 (**Table S1B**).

(**E***ii*) The CagA status by ELISA among 317 out of 322 Kalixanda individuals (5 individuals were not tested for CagA) exhibited strong correlation with IT50, with a median IT50 = 11 for CagA-negative individuals and a median IT50 = 40 for CagA-positive individuals. *** $p < 0.001$.

(**E***iii*) The general immune response against *H. pylori* (ELISA) and IT50 among the 322 Kalixanda individuals showed no correlation.

(**E***iv*) A rank correlation test showed that the IT50s increased with age among the 322 Kalixanda individuals, $r = 0.28$, $p \leq 0.000045$. This was most similar to a regular correlation test, $r = 0.18$, $p \leq 0.001$.

(**F***i*) The IT50s of 79 ELISA-positive individuals from Sumy, Ukraine, tested with strain 17875/Leb with a median IT50 = 69 and a mean IT50 = 125, where 44 (56%) sera samples were positive for Leb inhibition by strain J166 (**Table S1C**).

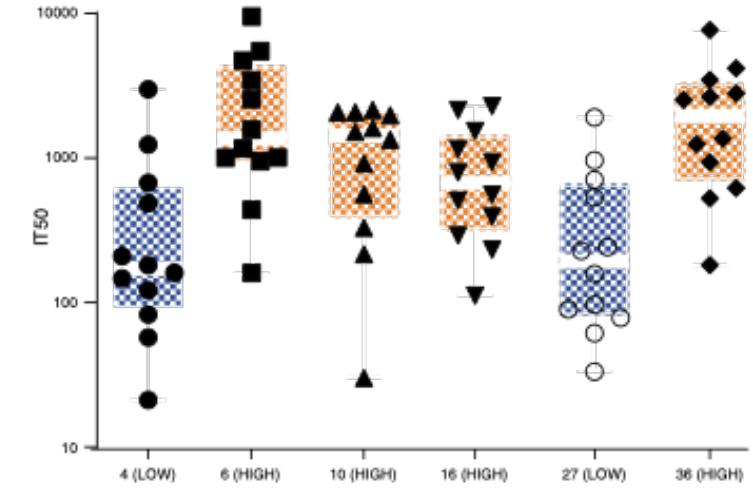
(**F***ii*) The IT50s of 141 ELISA-positive individuals from the US tested with strain 17875/Leb with a median IT50 = 39 and a mean IT50 = 79, where 83 sera samples (59%) were positive for Leb inhibition by strain J166 (**Table S1D**).

(**F***iii*) The IT50s of 200 ELISA-positive individuals from Mexico City, Mexico, tested with strain 17875/Leb with a median IT50 = 50 and mean IT50 = 115, where 146 sera samples (72%) were positive for Leb inhibition by strain J166 (**Table S1E**).

(**G**) The 30 Mexican sera and corresponding strains (**Table S2B**) were tested for correlation between IT50s and the Leb binding property. Low IT50 (<16) sera are in orange and high IT50 sera (≥16) are in blue with medians indicated (Wilcoxon $p = 0.036$).

(**H**) Immunoblot detection by serum samples from (1) the Karolinska University Hospital (Sweden) (**Figure 1I**), (2) Ukraine, (3) the US, (4) Mexico, (5) the Kalixanda series (Sweden), and (6) the ELISA-negative individual 5 from **Figure 1A**. BabA protein was purified from strain 17875/Leb and separated by semi-native SDS-PAGE (samples were kept at 37°C for 10 min without reducing agent) or under full denaturing and reducing conditions (samples heated to 100°C in reducing SDS sample buffer with 8M urea and 10 mM DTT). BabA binding by sera antibodies was detected using HRP-conjugated anti-human antibody.

A



B

Strain			ABO Blood Group Antigen Binding Properties, %			Binding Preference[a]
Continent	Country	ID	Leb, Hot	Leb, Cocktail	ALeb, Cocktail	
Reference		17875/Leb	97[b]	32	29	Generalist
		J166	25[b]	12	16	Generalist
Europe	Sweden	Sw44[c]	42	47	33	Generalist
		Sw103	93	24	14	Generalist
	Spain	S864	83	23	16	Generalist
Asia	India	I9	64	15	9	Generalist
	China	Ch1	86	44	36	Generalist
	Japan	J533	88	27	26	Generalist
North Americas	USA/Alaska	A714	89	23	21	Generalist
		A723	63	11	0.3	Specialist
South Americas	Peru	P330	88	28	0.3	Specialist
		P436	86	49	12	Specialist

C

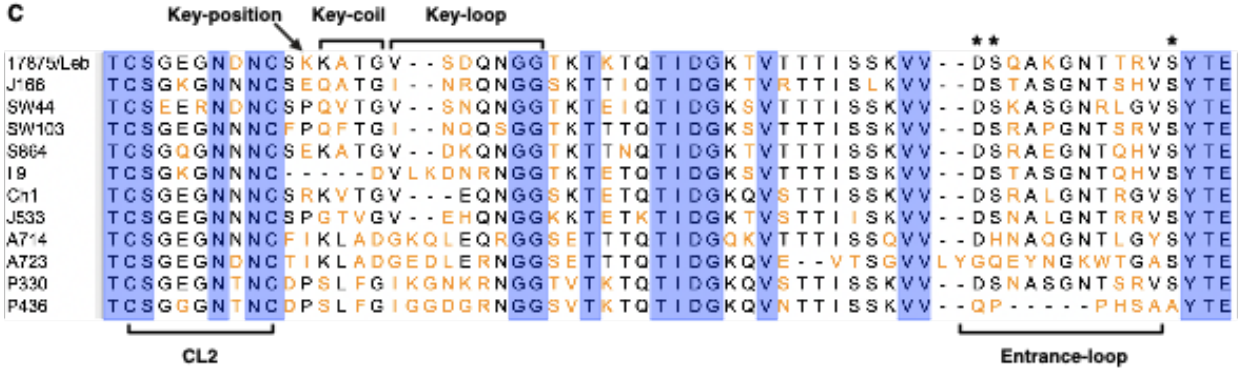
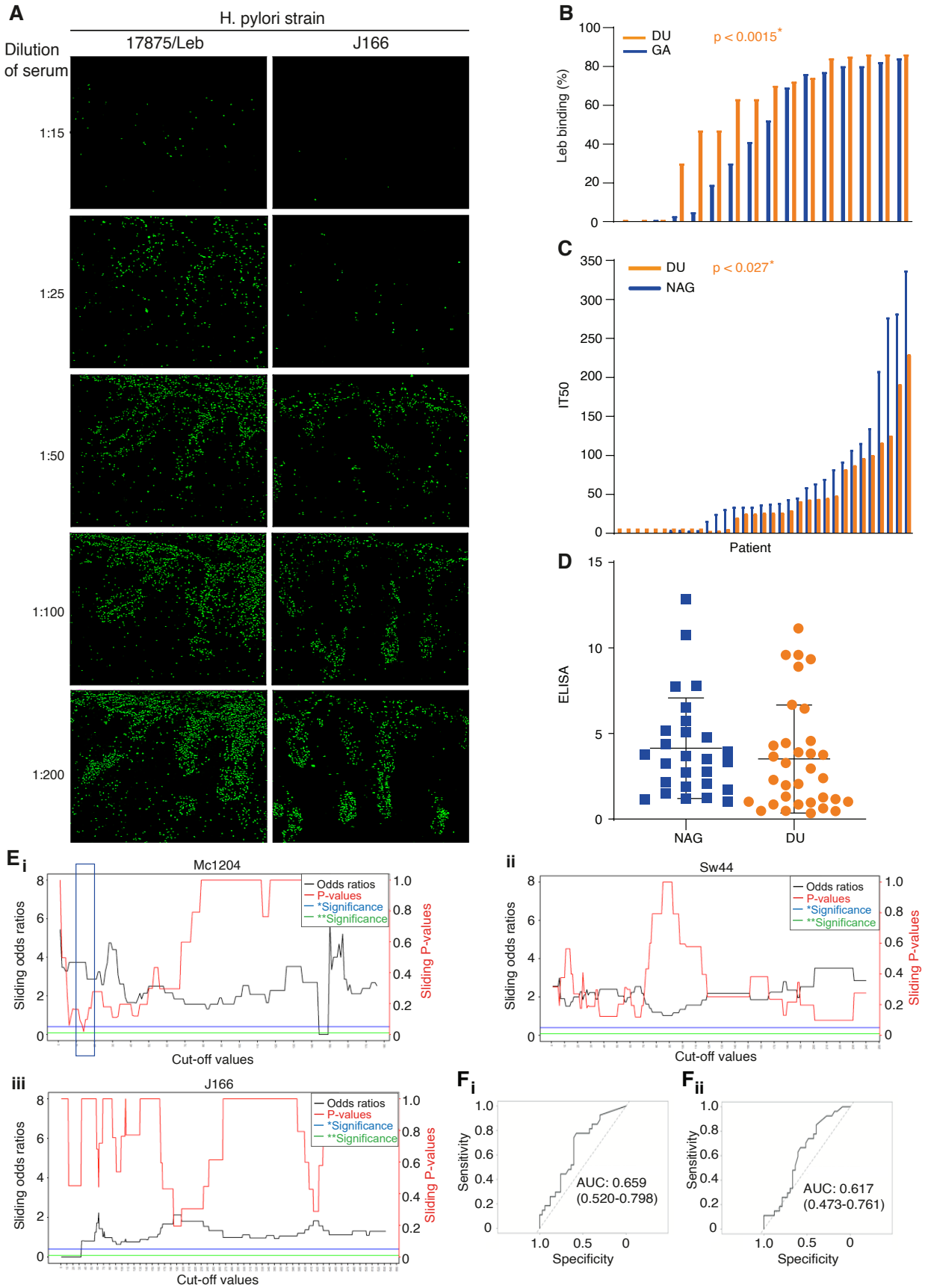


Figure S2. The broadly blocking serum Abs

(**A**) A box-plot presentation of the IT50 titers for the 12 strains in **Figure 2A** showing the relatively higher variation in IT50 titers for the two lower-inhibitory sera (LOW in blue, individuals 4 and 27) compared to the four sera with Higher inhibitory titers (HIGH in orange, individuals 6, 10, 16, and 36). In the log-scale presentation, the IT50 titers demonstrate increased spans between the quartiles for the LOW serum samples (Ansari-Bradley p = 0.07, i.e., close to significant and significant by removal of one outlier and between the "highest" from the LOW sera and the "lowest" from the HIGH sera (Ansari-Bradley p = 0.029). The results suggest that the LOW sera displayed a higher level of discrimination for different strains compared to the HIGH sera that efficiently blocked the Leb binding of the majority of *H. pylori* strains.

(**B**) Binding properties and binding preferences of *H. pylori* strains tested for inhibition by human sera (**Figure 2A**) and by ABbA (**Figure 4A**). [a]The Indigenous South American specialist isolates bind to Leb much better than to ALeb (from 2.5-fold to ~100-fold), i.e., there is a Specialist preference for binding to blood group O antigen. In comparison, the common Generalist binding preference is defined as the Leb/ALeb-ratio interval from 1:1 to 1:2.5 [11]. [b]The Hot Leb binding is from **Figure S1D**. [c]The ABO/Leb binding preference of *H. pylori* Sw44 is described in [11].

(**C**) Alignment of the central part of the BabA CBD of the *H. pylori* isolates from **Figure 2A.** The strains were chosen with respect to differences in Leb-binding affinity, binding preference (ABO-Generalists *vs.* O-Specialists), and BabA phylogeny, illustrated in (B) [11,14]. The stars indicate the locations of the conserved Leb-binding DSS triad residues [13]. However, exceptions do exist, and the DSS residues in the BabA Entrance loop that are critical for binding to ABO/Leb can be modified by a change of charge or hydrophobic substitutions or by deletions, e.g., in the Specialist strains that only bind to the blood group O antigen, which is a common adaptation in binding preference among Indigenous American/Latin American strains such as A723 and P436 [11,13].



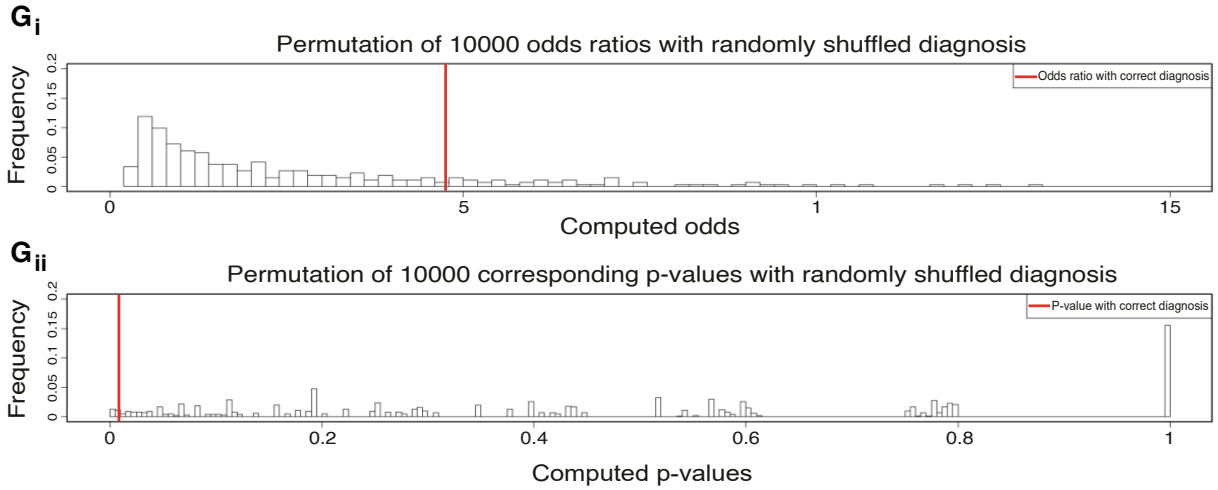


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Figure S3. Broadly blocking serum Abs protect against overt gastric disease

(A) Strains 17875/Leb and J166 were tested for blocking of *in vitro* binding to human gastric mucosa (**Figure 2B**) by a dilution series of sera from individual 1 (from **Figures 1A** and **1B**). Attached bacterial cells were quantified by ImageJ.

(**B**) A series of 32 Mexican isolates from patients with GA or DU (16 isolates for both) were tested for Leb binding strength with 1 ng of ^{125}I-labeled Leb-conjugate, i.e., a limiting concentration, defined as "Hot-Leb". The DU isolates demonstrated generally higher binding strength compared to GA isolates (Wilcoxon signed-rank test, $p = 0.0015$) (**Table S2B**).

(**C**) The 79 serum samples from NAG and DU patients demonstrated generally higher IT50 for patients with NAG ($p < 0.027$) (**Table S3**).

(**D**) The 79 Mexican serum samples from patients with NAG or DU did not show significant differences in *H. pylori* ELISA, $p < 0.4$, i.e., the two patient groups exhibited similar general immune responses against chronic *H. pylori* infection (**Table S3**).

(**E***i*) Sliding window for strain Mc1204; critical IT50 = 15 and $p < 0.0189$* (indicated by the box) (**Table S3**).

(**E***ii-iii*) Sliding windows for strains Sw44 (ii) and J166 (*iii*), i.e., strains that are less discriminative for high *vs*. low-inhibition titers and thus do not provide the critical IT50 values with significant ORs (**Table S3**). Our approach using high *vs.* low-affinity binding strains is conceptually similar to tests with different mAbs for discrimination between sensitivity and specificity in epitope recognition. The high-affinity strains 17875/Leb (**Figure 3C**) and Mc2014 (**Figure S3E***i*) discriminate between high *vs.* low IT50 in contrast to the low-affinity binding strains J166 and Sw44 (**Figure S2B**), which do not produce significant ORs (***ii*** and ***iii***). However, the low-affinity binding strain J166 identified all IT50-positive serum samples with low IT50 *vs.* the true IT50-negative sera samples (**Table S3**).

(**F***i*) The ROC diagram AUC 0.659 for strain 17875/Leb shows that the critical IT50 value that provides the highest significance is 29.5, i.e., the Youden index using the Area Under the Curve (AUC) where sensitivity and specificity are maximal. The described approach for finding optimal cut-offs using the OR as the discrimination measure can be seen as complementing a more common approach, namely that of using the Youden index while showing the overall classification performance across all possible cut-offs using an ROC curve and associated AUC. The optimal cut-offs identified using this approach are very similar, and we can thus view the "OR approach" as a way of illustrating the classification performance across the range of possible cut-offs. This complements the AUC, which gives a measure of overall classification performance. What we see using the OR approach is that the best classification performance (high ORs) is achieved within a narrow range of IT50 values around 30, i.e., where an optimal cut-off is located. This, together with the AUC value provided in the ROC, indicates that there is indeed useful information in the IT50 values. The ROC analyses were performed using the *pROC* package in R [62].

(**F***ii*) The ROC diagram AUC was 0.617 for strain Mc1204, and the critical IT50 value was 15.5.

(**G**) To verify the OR approach in an unbiased manner, we performed permutation tests where, in each iteration, we randomly permuted the outcome labels NAG/DU and then searched for an optimal Rf IT50 and its associated OR and its corresponding significance (p-value). We performed 10,000 iterations in each of these two permutation tests, and the F*i*-test showed that the number of ORs (i.e., classification performance) that exceeded

OR 4.75 (red bar, from **Figures S3B** and **3C**) were less than 2% of the permutation test iterations. In addition, a **G*ii*-test** showed that the ORs with high corresponding significance (p-values) constituted non-random results ($p = 0.027$ and $p = 0.0197$, respectively).

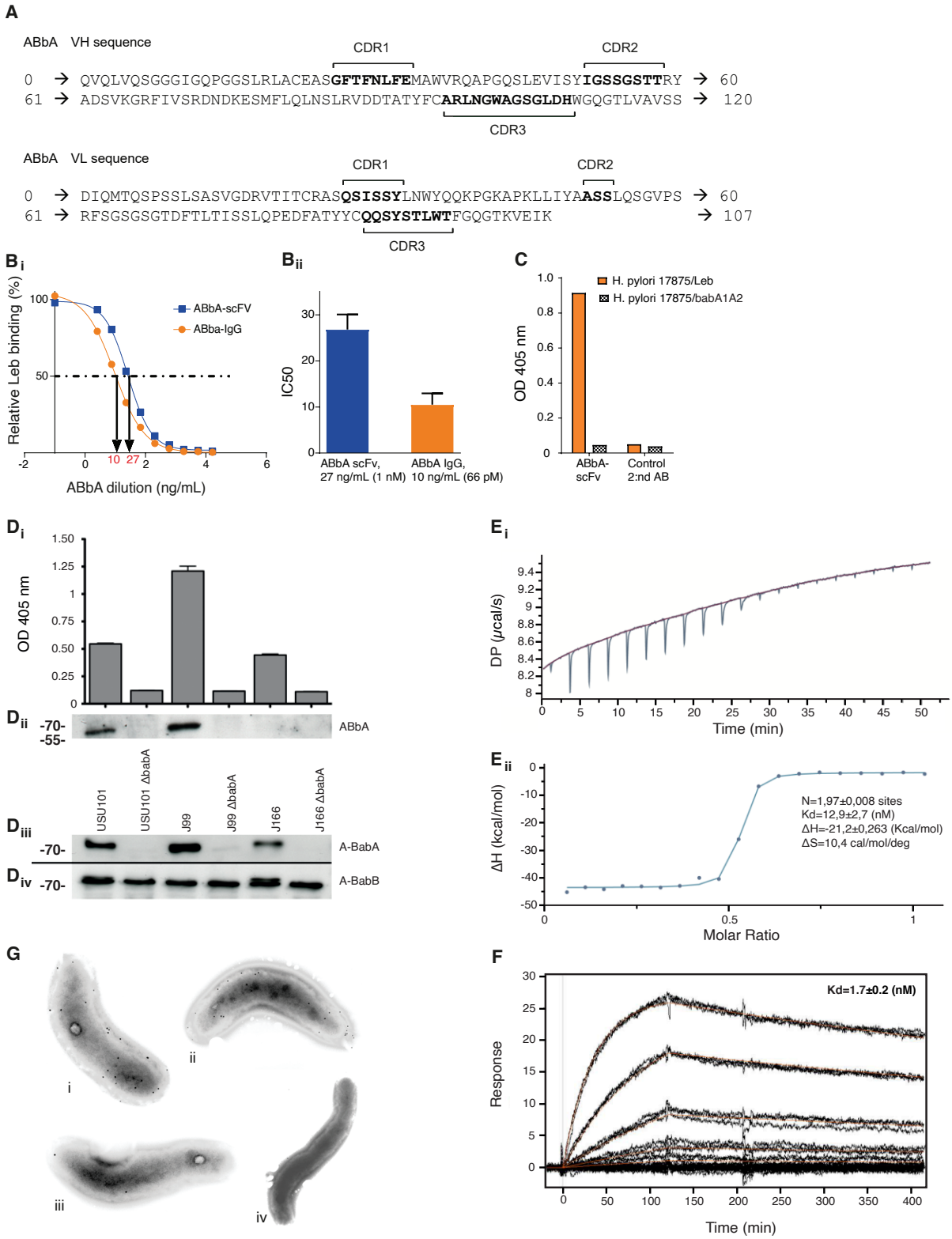


Figure S4. Cloning and identification of ABbA, the broadly blocking mAb

(A) Amino acid sequences of the ABbA VH and VL. The ABbA-VH region was generated by recombination of the germline gene IgHV3-48*3 with the D segment of IgHD2-15*01 and the J segment of IgHJ4*03. The high number of mutations in comparison to the germline gene indicates intense affinity maturation. The ABbA-VL chain was derived from the VL germline gene IgGKV1D-39*01 by recombination with the J segment of IgKJ1*01. Interestingly, the ABbA-VL chain was nearly identical to its most closely related germline gene.

(B*i* and B*ii*) Binding strength of ABbA(1)-scFv (27 kDa) *vs.* ABbA-IgG (ABbA) (150 kDa) by strain 17875/Leb with a 16-fold difference in IC50 (the concentration of antibody that inhibits *H. pylori*-Leb binding by 50%) of 27 ng/mL (1 nM) and 10 ng/mL (66 pM), respectively.

(C) Specificity of ABbA binding. ABbA(1)-scFv binds to *H. pylori* 17875/Leb but not to its isogenic 17875*babA1A2*-minus strain. ELISA wells coated with the two *H. pylori* strains were incubated with ABbA(1)-scFv. Binding was detected using an anti-myc mAb and HRP-conjugated anti-mouse Ab, and the control was secondary Ab only.

(D) Detailed specificity in ABbA binding. To test for cross reactivity with the non-Leb-binding paralog BabB protein (with unknown function), three strains – USU101 (https://www.ncbi.nlm.nih.gov/nuccore/NZ_CP032818.1) and J166 from central/southern Europe [22] and J99 of African phylogeny [40] (**Figure 2B**) – and their *babA*-minus mutants – were analyzed. Two spontaneous *babA*-minus mutants, USU101Δ*babA* and J166Δ*babA,* isolated after passage from Rhesus macaques [44,63], and a J99Δ*babA* genetic deletion mutant [41] were compared with their cognate BabA-positive parent strains. (***i***) ELISA wells coated with the three *H. pylori* strains and the corresponding *babA*-minus mutants were incubated with ABbA-IgG. Binding was detected using an HRP-conjugated anti-human antibody. (***ii***) Immuno-blot detection of BabA by the strains USU101, J99, and J166. ABbA-IgG recognizes and binds BabA but does not recognize any bands/proteins in the BabA-negative strains. The lower affinity of J166 for ABbA binding is reflected in the binding of ABbA-IgG to BabA on the bacterial surface in the ELISA, but not to semi-denatured BabA on immunoblots. The ELISA was repeated three times, and each bar represents the mean of three values with the standard error. (***iii***) BabA expression was verified in an immunoblot with BabA-specific rabbit serum under denaturing conditions, where BabA was expressed in the original strains but not in the corresponding isogenic BabA mutants. (***iv***) BabB expression was verified in an immunoblot with BabB-specific rabbit serum under denaturing conditions, where all tested strains expressed BabB. The BabA protein was detected with VITE rabbit antibody [14], and BabB was detected by VIRA rabbit antibody diluted 1:6000 and secondary HRP-goat (anti-rabbit) antibody diluted 1:1000 (DakoCytomation, Denmark A/S).

(E) Affinity of ABbA-IgG. (*i*)The ABbA-IgG binding affinity to recombinant soluble BabA (527 aa) devoid of the membrane-spanning hydrophobic beta-barrel domain was measured using isothermal titration calorimetry (ITC). **(*ii*)** Five separate ITC tests demonstrated an affinity of 10.2 ± 1.5 nM with one representative experiment of Kd = 12.9 nM shown in the figure.

(F) ABbA-IgG was immobilized on a chip and tested by Biacore Surface Plasmon Resonance (SPR) for binding to soluble BabA. Three separate tests demonstrated a Kd = 1.7 ± 0.2 nM. Most likely, the functional binding strength of ABbA-IgG will be log-folds

increased by the avidity effects gained in binding to BabA multimers on the *H. pylori* bacterial surfaces [14].

(G) Immuno-electron microscopy demonstrated specific BabA immune staining of *H. pylori* by ABbA. Bacterial cells with *H. pylori* 17875/Leb (***i***, ***ii***) were incubated with ABbA, and bound IgG was visualized with 10 nm gold-labeled protein A. The 17875*babA*-minus mutant was used as a negative binding control (***iii***), and the anti-E2 HCV envelope IgG1 was used as a negative antibody control (***iv***). The 17875*babA* mutant displayed only non-specific background binding similar to the isotype control antibody.

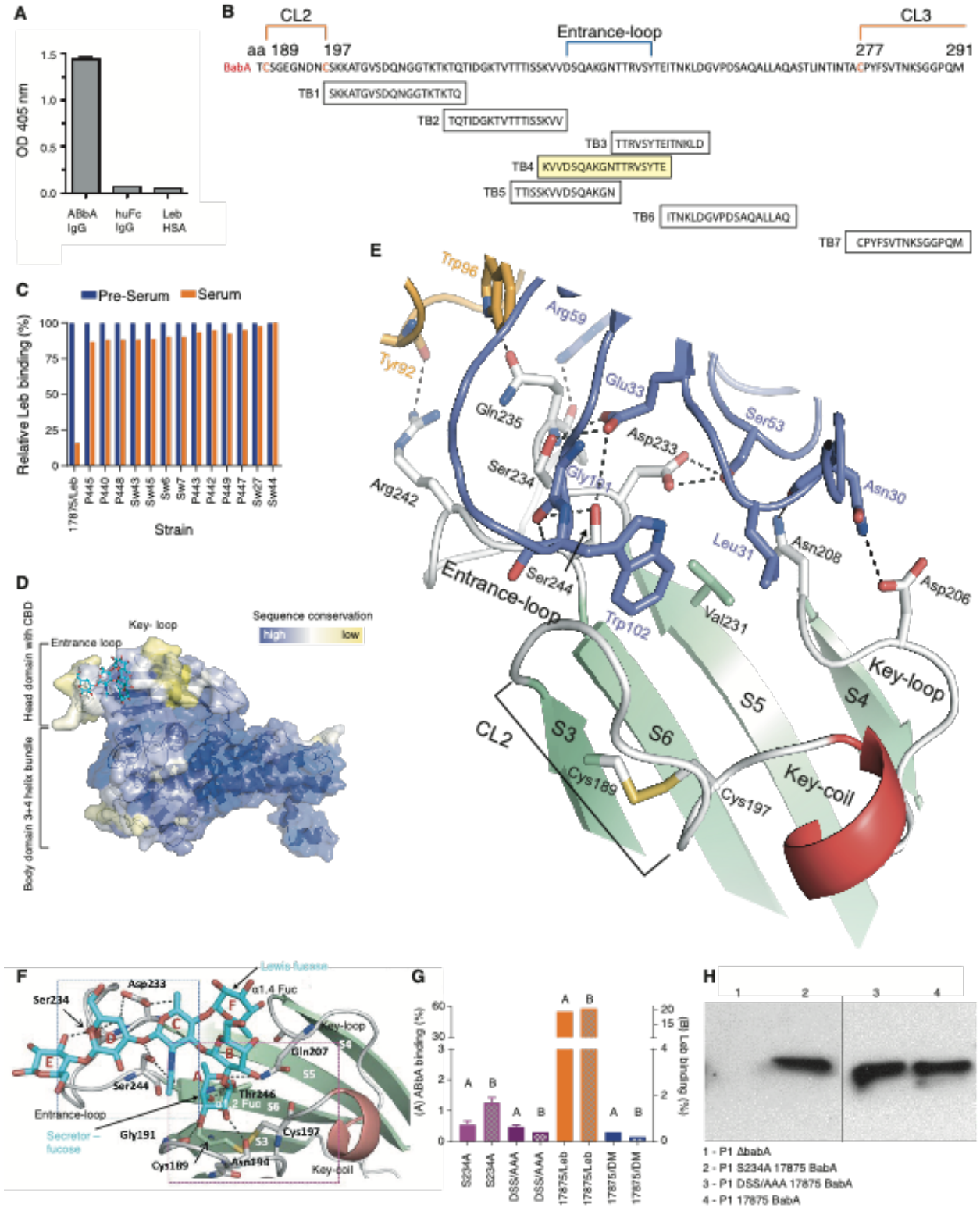


Figure S5. Identification of the structural binding epitope in BabA for the broadly blocking ABbA

(**A**) The 260 aa $BabA_{76-335}$ polypeptide selected from the phage-display shotgun library was recombinantly expressed with its three disulfide loops. Binding was assessed by ELISA with ABbA-IgG and human Fc (IgG1) fusion protein (as the negative control) and Leb (as the receptor). The 260 aa BabA fragment comprises an adequate epitope for ABbA binding but does not provide sufficient structural stability and support for Leb binding. The 260 aa BabA fragment was identified as reviewed in [64].

(**B**) Alignment of the seven synthetic peptides of the CBD domain from aa197 to aa291, where peptides TB2, TB3, TB5, and TB6 partially overlap peptide TB4.

(**C**) Inhibition of Leb binding by the rabbit-sera TB4 of a series of *H. pylori* strains from Sweden (Sw) and Peru (P) and strain 17875/Leb. The TB4 serum, which was derived from the TB4 peptide of strain 17875/Leb, only efficiently inhibited Leb-binding by strain 17875/Leb and did not significantly inhibit Leb-binding of strains from geographically local Sweden or distant Peru.

(**D**) The BabA adhesin exhibits extensive polymorphism with multiple amino acid substitutions (indicated in yellow) preferentially focused in the Entrance loop and the Key Coil/Loop in the CBD, which is located in the head domain [14].

(**E**) For clarity, the co-crystal structure shows the ABbA-BabA interaction without Leb. Out of 15 bonds in total, the VL makes 3 bonds with the Entrance-loop and the VH makes the other 12 bonds, including the triple glycan mimicry (GM) domains. The BabA (grey loops and green β-strands) bound to ABbA-Fab (VH in lilac, VL in beige) with the amino acid residues that bind BabA indicated, including the hydrophobic W102 and L31 that substitute for the fucose residues. In addition, VH residues E33, S53, and G101 (in blue) form tight grips with the DSS triad. The VL also contributes with bonds to R242 and Q235. Q235 also binds to R59 in the VH and thus is the only BabA residue that binds to both the VH and VL.

(**F**) Structure of the 17875 BabA-CBD bound to and co-crystallized with Leb (Leb shown in cyan; PDB: 5F7W). The six sugar rings of Leb are indicated by A–F, where A and F are the secretor fucose and Lewis fucose, respectively, making α1.2 and α1.4 bonds with the Gal (B) and GlcNAc (C), respectively. The D and E residues constitute the lactose core and together with GlcNAc (C) form H-bonds (dashed lines) with the DSS residues located in the BabA Entrance loop. The secretor fucose makes many bonds with the CL2 loop, whereas the Lewis fucose interacts with the hydrophobic V231 residue located in the immediate proximity of the DSS triad [13].

(**G**) The triple DSS-to-AAA mutant and the critical single S234A DSS mutant of BabA were expressed in *H. pylori* strain P1Δ*babA,* where they demonstrated loss of both ABbA and Leb binding. Controls were the 17875/Leb BabA expressed in the P1Δ*babA* strain (positive control) and the 17875*babA1A2*-minus mutant (negative control).

(**H**) BabA expression was verified by two (fused) immunoblots by BabA rabbit sera and showed that the expression level of BabA 17875/Leb in the *H. pylori* P1-DSS/AAA and P1-S234A mutant was similar to that of *H. pylori* P1 with the non-mutated BabA.

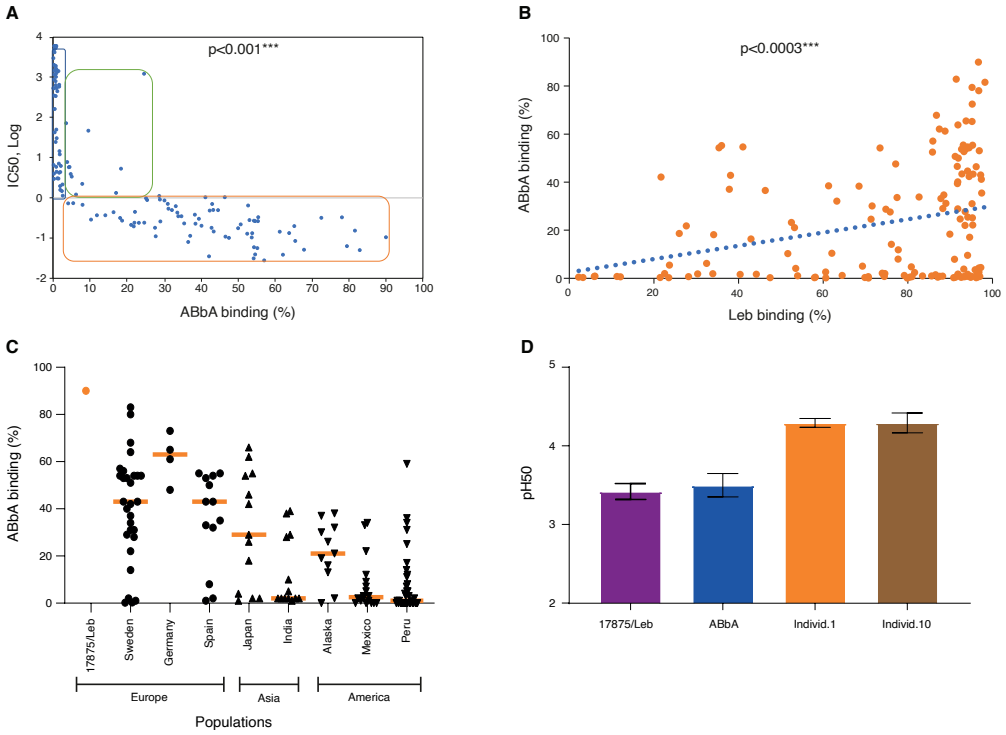
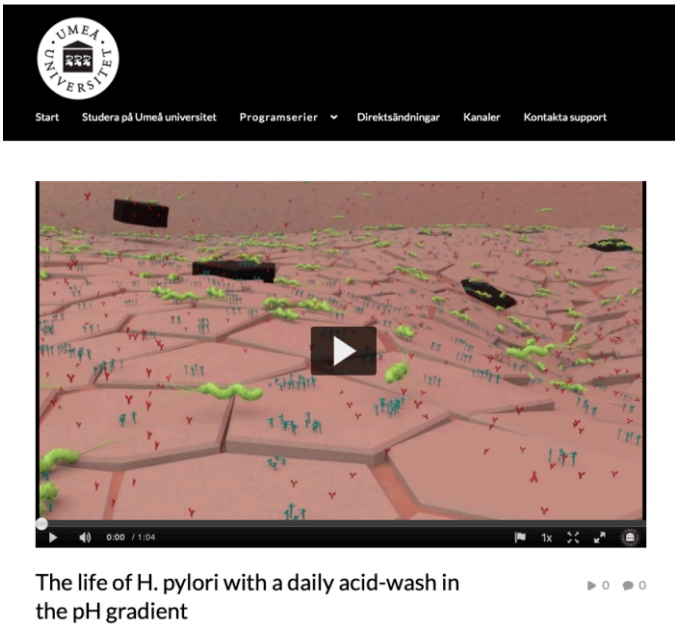


Fig 6. The ABbA global binding epitopes and their acid sensitivity in binding.
(A) The ABbA-IgG binding strength showed a strong correlation with the ABbA IC50 (**Table S7**). Spearman's rank correlation r = –0.881 ($p < 0.001$).
(B) The ABbA and Leb binding strengths (**Table S7**) strongly correlate among global strains ($r_s = 0.3$, $p < 0.0003$). Thus, clinical isolates with higher binding strength for Leb most often bind ABbA-IgG with higher binding strength.
(C) The ABbA-IgG binding strength is higher among European strains and also among strains from Japan, whereas strains from Southeast Asia (India) and North, South, and Latin America are lower in ABbA binding strength.
(**D**) The acid sensitivity profiles, denoted as a pHgram, were determined by incubation of *H. pylori* with 125I-labled Leb and ABbA-IgG and Fc-purified IgG antibodies from individuals 1 and 10 in the pH 6–2 interval [14]. The series of pH50s were repeated 3 times with SEMs. The test also showed that ~1% of the purified serum IgG bound to *H. pylori*, i.e., 0.1 mg/mL out of 10 mg/mL IgG. With this new understanding that the bbAb/ABbA content is 1/10,000 part of the IgG pool (**Figure 4D**), we conclude that bbAb similarly to ABbA constitutes ~1% of the serum IgG in circulation that binds to *H. pylori*.



Video S1. https://play.umu.se/media/t/0_bf1lh9gt

The life of *H. pylori* with a daily refreshing acid wash.

The gastric onco-pathogen *H. pylori* lives in the stomach lining, referred to as the gastric epithelium. Close to the epithelial cells, the viscous mucus layer provides a bicarbonate buffer zone that protects the epithelial cell lining from the acidic gastric juice present in the stomach lumen just a third of a millimeter away. However, as the distance from the cell lining increases, the bicarbonate buffering fades to form a pH gradient that extends about half-way up the mucus layer. At this “altitude”, the impact of the very acidic gastric juice drops the pH back to pH1–2. The gastric juice is acidified by hydrochloric acid, which of course is too acidic for most microbes, *H. pylori* included. In this fascinating environment, *H. pylori* has adapted its life in the stomach to make life-long use of both the epithelial cell lining and the mucus layer pH gradient [14,26]. The more virulent *H. pylori* isolates bind the ABO blood group antigens (in blue) on the epithelial cell surfaces for firm bacterial attachment. In this prime location, *H. pylori* has full access to the necessary nutrients and iron leaching from the mucosal cells. However, pros come with cons, and the tight attachment exposes *H. pylori* to our immune system. The *H. pylori* infection is a major target of the humoral immune system, and the majority of carriers produce ELISA titers against *H. pylori* antigens. Hence, the *H. pylori* infections are exposed to high levels of antibodies (in red) that disseminate into the gastrointestinal tissues from the systemic circulation as well as from antibody-producing cells in both the stomach and gut lining. These antibodies bind to a plethora of *H. pylori* antigens such as the urease enzyme, LPS, heat-shock proteins, and the CagA effector protein. Although, the very best attempt possible by our immune system, the antibodies against *H. pylori* never manage protect against the *H. pylori* infection, which instead establish itself through adaptation and persists over the lifespan. The persistent infection is the cause of the chronic mucosal inflammation that in many millions of cases annually results in gastric disease, although of different degree of severity, ranging from mild and non-atrophic gastritis to “the silent killer” gastric cancer.

Our results suggest that the humoral immune system has found a way to balance the inflammation pressure by raising the bbAbs that prevent BabA adhesin from binding to

the ABO/Leb glycans. Thus, the bbAbs block or reduce attachment of the *H. pylori* bacteria to the cell surfaces in the epithelial lining. The bbAbs bind to folded structures in the carbohydrate binding domain (CBD) of the BabA attachment protein (the green hooks). This is illustrated by the *H. pylori* bacterial cell (located in the center) that is blocked by the bbAbs in binding the ABO glycans by the full set of BabA adhesins. Similarly, the bacterium to the left carries a multitude of bbAbs at its right pole and is barely hanging on in attachment to the cell surface ABO antigens.

To avoid detrimental consequences of the humoral defense and complement system activation, *H. pylori* can take advantage of the rapid gastric mucosal desquamation process, where epithelial cells are pushed into the mucus layer pH gradient. This is a natural, essential, and innate immune protective process and the epithelial cells undergo rapid turnover every 2–3 days and are continuously replaced with new cells proliferating from the stem cells located in the column-palisade just below. The protective mucus layer is renewed even faster, about twice per day. If these processes were irreversible and sufficient, the desquamation process would move and transport all attached *H. pylori* bacterial cells to the gastric juice where the bacteria would be destroyed by the acidic environment. If this were the case, the *H. pylori* infection would be naturally eradicated in a week or maybe two. But this does not take place and instead *H. pylori* adapts to the host and successfully persists for the lifetime of the individual.

Our new results suggest that *H. pylori* does not merely and passively adapt to the desquamation process but instead actively makes good use of it as a way to escape the humoral immune system. As the *H. pylori* cells that are attached to desquamating cells move upwards and through the mucus layer, they soon reach their first rejuvenation region at ~pH 4.5, where the majority of acid-sensitive antibodies and complement molecules are both de-attached and inactivated. After about 2 h and further out in the mucus layer, at the slightly lower pH 3.5, the *H. pylori* cells will rid themselves also of the more acid-resistant bbAbs.

But how do the *H. pylori* manage to detach from the desquamating cells? The BabA adhesin binds to the ABO/Leb antigens on the cell surface similarly to the glycan mimicry of the bbAbs. During the millennia of adaptation to the human gastric mucosa, the main attachment protein BabA has evolved to be acid sensitive in its binding to ABO/Leb blood group glycans. At the low pH 3.5, the majority of BabA no longer bind, and the *H. pylori* will come loose from the desquamating cells. Once free, “acid-washed”, and again fully motile, *H. pylori* uses its chemotactic sensors and flagella (Goers Sweeney *et. al, Structure*, 2012) to propel itself along the pH gradient from the epithelial cells back to the buffered epithelial surface by its reported rapid motility in the mucus zone [65], *H. pylori* can in a short time return to the less acidic parts of the epithelial lining, where the bacteria cells can again reattach in a continuous recycling process. Thus, by taking advantage of the pH gradient, the *H. pylori* infection can escape the humoral effector molecules of the immune system and, in addition, can recycle the infection through natural bio-selection of those bacterial cells that have introduced mutations or induced or modified expression patterns that are the best suited for life in the local gastric environment. This also allows for adaptation to changes over the lifetime of the host. However, long-term infection by adherent *H. pylori* that cause chronic mucosal inflammation constitute the critical risk for gastric cancer development.

Supplemental Tables

Table S1A-F related to **Figures 1** and **S1** and **2** and **S2** and **3.**
Characteristics of Individuals from Karolinska University Hospital, Sweden; Kalixanda Study, Sweden; Sumy Regional Clinical Hospital, Ukraine; Baylor College of Medicine, Houston, TX, USA; Mexico UMAE Pediatria, Mexico City, Mexico; Regional Children Hospital and St. Zinaida City Children Hospital, Sumy, Ukraine.

Table S2A-B related to **Figures S1G** and **3A** and **S3A.**
Leb-binding properties of Swedish and Mexican strains.

Table S3 related to rest of **Figures 3** and **S3**.
Sera IT50 from Non-Atrophic Gastritis (NAG) and Duodenal Ulcer disease (DU) patients.

Table S4 related to **Figures 1** and **3** and **S1**
The location of the IT50 = 30 interval in the different cohorts as identified by strain 17875/Leb, and the location of IT50 positive *vs*. negative sera in the different cohorts identified by strain J166.

Table S5. Crystallographic data collection and refinement statistics for the BabA protein co-crystallized with ABbA.

Table S6A. Binding properties and IC50 of Eurasian *H. pylori* strains.
S831, I109, and I119 are marked in red as the Specialists among 49 European and 27 Asian strains.

Table S6B. Binding properties and preferences and IC50 of North and South Indigenous American and Latin-American *H. pylori* strains.
ND - Not Determined
O - Specialists are the strains with >2.5 ratio in Leb/ALeb binding [11].
A - Specialists are the strains with <0.4 ratio in Leb/ALeb binding [11].

Table S7. BabA alignment (aa 180–250) according to ABbA binding strength. Sequences that originated from [11] are indicated by a star (∗).
Sequences that originated from [14] are indicated by a triangle (∆). Mexican Mc1215, Mc1207, and Mc1227 were sequenced by the J. Torres lab (co-author).

Table S8. ABbA binding properties of global *H. pylori* strains and of generalist vs. specialist *H. pylori* strains.

Table S1A, related to **Figure 1** and **Figure S1, Figure 2** and **Figure S2** and **Figure 3. Characteristics of *H. pylori* ELISA-positive individuals from Karolinska University Hospital, Sweden.**

#	Serum Code	IT50 17875/Leb
1	Individual 1	0
2	Individual 2	0
3	Individual 3	10
4	Individual 4	252
5	Individual 5	20
6	Individual 6	1643
7	Individual 7	448
8	Individual 8	0
9	Individual 9	0
10	Individual 10	2168
11	Individual 11	17
12	Individual 12	0
13	Individual 13	0
14	Individual 14	0
15	Individual 15	0
16	Individual 16	1280
17	Individual 17	9
18	Individual 18	6
19	Individual 19	0
20	Individual 20	0
21	Individual 21	0
22	Individual 22	0
23	Individual 23	20
24	Individual 24	141
25	Individual 25	132
26	Individual 26	157
27	Individual 27	674
28	Individual 28	0
29	Individual 29	0
30	Individual 30	59
31	Individual 31	107
32	Individual 32	0
33	Individual 33	7
34	Individual 34	51
35	Individual 35	14
36	Individual 36	2041
37	Individual 37	0
38	Individual 38	43

Table S1B related to **Figure 1** and **Figure S1** and **Figure 3**.
Characteristics of Individuals from Kalixanda Study, Sweden.

The serum samples are displayed according to IT50s tested with *H. pylori* strain 17875/Leb. In addition, *H. pylori* strain J166 identified the series of IT50 titers as positive (+) or negative (–). The location for the background level (the start of the positive IT50 sample is indicated by the horizontal bar) was calibrated with sera from ELISA-negative individuals using *H. pylori* J166.

#	Serum Code	Sex	Age	ELISA		IT50	
				H. pylori	CagA	17875/Leb	J166
322	K1260	F	67	116.9	1	1314	+
321	H1959	M	66	47.7	1	931	+
320	H87	F	76	127.8	1	748	+
319	K1047	F	71	77.8	1	564	+
318	K275	M	72	103.9	1	489	+
317	H2529	M	40	120.3	1	461	+
316	K1384	M	60	103.5	1	458	+
315	K1421	F	64	107.1	1	427	+
314	H2821	F	65	88	1	416	+
313	H1376	F	74	58.9	1	376	+
312	K2789	M	47	36.5	0	355	+
311	H2441	F	51	108.6	1	343	+
310	K2593	F	78	124.8	1	329	+
309	K2787	M	77	119.5	1	321	+
308	H2905	M	62	117.3	1	305	+
307	H2181	M	62	112.8	1	297	+
306	H824	F	44	119.8	1	294	+
305	K49	M	74	72.9	0	292	+
304	H244	M	44	15.2	1	280	+
303	K1999	M	82	92.6	1	259	+
302	K1488	M	58	123.9	1	255	+
301	H1218	F	70	98.5	1	250	+
300	H2162	M	39	21.1	1	243	+
299	H278	M	72	106.8	1	236	+
298	K1614	M	65	100.5	1	234	+
297	H2574	M	72	48.3	1	230	+
296	K2498	F	62	113.6	0	206	+
295	K2608	M	32	125.8	1	199	+
294	H2854	F	67	116	1	194	+
293	K1415	M	66	17.1	1	186	+
292	K956	M	66	103.9	1	186	+
291	K15	F	53	128.3	1	185	+
290	H988	F	67	56.6	1	180	+
289	K2600	F	77	27	1	179	+

288	K2644	F	56	116.8	1	173	+
287	H814	F	52	109.2	1	170	+
286	H2000	F	59	106.3	1	168	+
285	K2042	F	72	130.7	1	161	+
284	H197	M	69	72.5	1	157	+
283	H18	F	57	41.9	1	153	+
282	K295	M	59	104.3	1	150	+
281	K1829	M	38	78.7	1	149	+
280	H1262	M	71	114.9	0	148	+
279	H812	F	25	27.2	1	145	+
278	H2876	M	35	113.5	1	145	+
277	H1833	F	64	113	1	144	+
276	K2026	F	70	91	1	138	+
275	H2842	F	80	121.1	1	137	+
274	H817	F	77	82.4	1	133	+
273	H2022	F	67	120.4	1	132	+
272	H1011	M	72	43.6	1	132	+
271	K2534	M	76	94.1	1	131	+
270	K1604	M	78	83	1	128	+
269	H1890	M	59	123.7	1	123	+
268	K2770	F	77	114.1	1	122	+
267	K1243	M	69	114.7		122	+
266	H853	F	73	145.3	1	120	+
265	H783	M	70	77.9	1	119	+
264	K745	F	73	130.9	1	119	+
263	K1953	M	53	98.9	0	118	+
262	H1517	M	64	105.3	1	116	+
261	K638	F	64	79.8	1	116	+
260	H2215	F	46	50.9	1	116	+
259	K364	F	67	94.2	1	115	+
258	K366	F	51	72.7	1	114	+
257	H2442	F	59	82.8	1	111	+
256	K450	F	76	48.9	1	110	+
255	H2924	F	54	117.7	0	110	+
254	K1650	M	74	101.1		105	+
253	H810	F	69	136.7	0	103	+
252	K681	F	68	121.2	1	102	+
251	H234	M	69	128.8	1	102	+
250	H1409	M	62	98.5	1	101	+
249	K1924	M	47	58.5	1	100	+
248	H262	F	71	46	1	100	+
247	H649	F	70	131.6	1	98	+
246	H2877	F	54	117.8	1	95	+
245	H1905	M	71	130.6	1	95	+
244	K1022	M	50	122.1	1	94	+

243	K2429	M	81	60.5	1	94	+
242	K1013	M	21	101.1	1	93	+
241	K299	M	51	116.3	1	93	+
240	K2462	M	80	20.5	1	92	+
239	K2090	F	43	134.3	1	91	+
238	K2765	M	62	72.6	0	91	+
237	K906	F	56	14.2	1	91	+
236	H1485	F	59	39.7	1	90	+
235	K1928	F	66	96.6	1	89	+
234	K2762	M	67	92.1	1	89	+
233	K1520	F	68	54.3	1	87	+
232	K135	M	53	65.8	1	85	+
231	K2030	F	64	89.9	1	82	+
230	K833	M	48	113.2	1	80	+
229	K2246	M	71	59.7	1	75	+
228	K2074	F	52	84.1	1	74	+
227	H2891	F	57	90.1	1	74	+
226	K1289	F	74	128.7	1	73	+
225	K1964	F	69	64	1	72	+
224	H1207	F	64	93.3	1	71	+
223	H2705	F	68	132.9	1	69	+
222	H1804	F	55	86.1	1	69	+
221	K1248	M	65	110.9	1	68	+
220	H718	M	62	68.9	1	66	+
219	K2156	M	40	40.8	1	66	+
218	H2012	M	75	101.6	1	66	+
217	K2570	F	76	83.6		64	+
216	H93	F	35	90.2	1	64	+
215	H2626	M	74	117.6	1	63	+
214	H907	F	63	119.9	1	63	+
213	H701	M	69	8.8	1	62	+
212	H926	M	75	131.9	1	62	+
211	K2132	F	63	97.8	1	62	+
210	H267	F	73	60.6	1	62	+
209	H1473	M	69	98.4	1	61	+
208	H2268	F	56	84.4	1	61	+
207	H1458	M	67	106.9	1	60	+
206	H840	M	67	92.5	1	59	+
205	K2067	M	39	75.5	1	59	+
204	K377	F	72	122.8	0	55	+
203	K959	F	61	135.8	1	54	+
202	K2783	F	52	52.4	1	54	+
201	H1247	M	71	91.8	1	53	+
200	K2840	F	57	66.7	1	53	+
199	H1391	M	36	64.2	1	53	+

198	H624	F	68	124.8	1	52	+
197	H964	F	35	36.6	1	52	+
196	K1294	F	78	87.1	1	50	+
195	K2606	M	63	127.3	0	49	+
194	K30	F	51	121.4	1	48	+
193	H2780	F	47	106	1	46	+
192	H1240	F	57	103.6	1	44	+
191	K2841	F	37	73.2	1	44	+
190	H1934	F	80	110.7	1	43	+
189	H1401	F	52	101.6	1	43	+
188	K2844	F	79	90.9	0	41	+
187	K1569	M	70	117.4	1	41	+
186	K2135	M	55	65.4	1	40	+
185	H2857	M	51	94	1	40	+
184	H2007	M	56	59.2	1	38	+
183	H118	F	28	79.9	1	38	+
182	K1073	M	73	105	1	36	+
181	K2878	M	61	74.5	1	36	+
180	H373	F	73	129.7	1	35	+
179	K2837	M	73	131.5	0	35	+
178	K326	M	59	92.2	1	35	+
177	H259	F	62	122.5	1	34	+
176	K2740	M	77	102.5	1	34	+
175	H690	F	57	81.1	1	34	+
174	H2450	F	79	79.9	1	33	+
173	K384	M	52	111.4	1	33	+
172	K2580	M	58	11.8	1	33	+
171	H157	M	65	139.8	1	31	+
170	H2811	M	50	91.1	0	30	+
169	H1351	M	51	74.6	1	30	+
168	H2260	F	78	113.8	1	28	+
167	K199	M	64	109.2	1	28	+
166	K731	M	68	122.3	1	27	+
165	K1117	F	47	13.9	1	26	+
164	H786	M	49	30.4	1	25	+
163	H1615	M	55	125.8	1	24	+
162	K2079	M	71	124.4	1	24	+
161	H2830	M	37	97.4	0	24	+
160	K381	M	60	110.6	1	24	+
159	K1880	F	63	99.4	1	24	+
158	K17	M	71	112	1	24	+
157	H1579	M	71	88.8	1	23	+
156	K1275	M	49	99	0	23	+
155	K105	F	45	71.7	1	22	+
154	H351	F	42	110	1	22	+

153	H2421	M	48	99.8	1	22	+
152	K2890	F	28	34.6	0	22	+
151	K2104	F	25	27.8	1	21	+
150	K2627	M	54	98	1	21	+
149	H57	F	66	80.3	1	20	+
148	H1560	M	56	116	1	20	+
147	H2806	F	77	82.1	0	20	+
146	H1949	F	72	98.5	1	20	+
145	K2540	F	74	99.1	1	19	+
144	K328	F	68	115	1	19	+
143	H2807	F	74	83.6	1	19	+
142	K430	M	55	81	1	19	+
141	H2618	M	45	131.6	1	19	+
140	H2700	F	64	108.9	1	19	+
139	K312	M	58	90.6	1	19	+
138	K993	M	70	120.8	1	19	+
137	K322	M	44	100.5	1	18	+
136	H2645	M	60	56.2	0	18	+
135	K56	M	64	87.2	1	18	+
134	K34	M	72	65.4	1	17	+
133	H2211	F	60	99.9	1	17	+
132	H2885	M	59	90	1	17	+
131	K2434	M	68	72.7	1	17	+
130	H303	F	45	77.9	1	17	+
129	K2164	F	67	26.3	1	17	+
128	K1807	M	56	115	1	17	+
127	K2718	M	48	90.6	0	17	+
126	K1966	F	68	114.7	1	17	+
125	K435	F	64	20.5	1	16	+
124	K632	M	52	126.3	1	16	+
123	H207	M	54	57.4	1	16	+
122	K416	F	62	117.1	0	16	+
121	K735	M	49	33.7	1	16	+
120	K1369	F	44	98.2	1	16	+
119	K279	M	39	106.9	1	15	+
118	H1212	F	65	64.1	1	15	+
117	H2206	M	47	23.4	1	15	+
116	H1078	F	38	79.2	1	15	+
115	K2478	M	41	87.2	1	14	+
114	H1551	F	56	118.6	1	14	+
113	H605	F	40	113.3	0	14	+
112	K2070	M	75	120.4	0	13	+
111	K892	F	68	82.6	1	13	+
110	H1375	F	37	135.2		13	+
109	K2526	M	55	108.9	1	13	+

108	K697	M	62	107.3	1	13	+
107	K2198	F	69	91.3	1	13	+
106	K1389	F	58	112.9	1	13	+
105	K1237	F	61	51.8	1	13	+
104	K2244	M	64	118.7	1	13	+
103	K395	F	43	110.8	1	13	+
102	K1292	F	75	78.3	1	13	+
101	H1426	M	58	109.7	1	13	+
100	K1425	M	44	108.5	0	13	+
99	H258	F	47	76.4	0	12	+
98	K28	F	67	117.3	0	12	+
97	H2829	M	73	64.9	1	12	+
96	K2951	M	62	135.7	0	12	+
95	K2118	F	58	32.3	1	12	+
94	H2886	M	32	25.5	0	12	+
93	H84	F	57	95	1	12	+
92	K1446	M	60	94.1	0	12	+
91	K2707	F	44	85.7	1	12	+
90	K2625	M	79	56.8	0	12	+
89	K940	F	53	115.3	1	12	+
88	H2180	F	59	94.5	0	12	+
87	K2464	M	49	118.4	1	12	+
86	K809	F	34	125.8	1	12	+
85	K2539	M	41	90.7	1	11	+
84	K966	F	60	44.4	1	11	+
83	K652	F	28	23.8	0	11	+
82	K59	M	50	126.9	1	11	+
81	H21	M	49	77.9	0	11	+
80	K2136	F	59	69.3	0	11	+
79	K1972	F	69	129.2	0	11	+
78	K2699	F	59	69.1	0	11	+
77	H2117	M	52	124.7	1	10	+
76	K2730	M	57	97.4	0	10	+
75	K83	M	53	92.4	1	10	+
74	K1427	M	30	62.8	1	10	+
73	H604	M	53	123.2	1	10	+
72	K2190	F	53	74.8	0	10	+
71	K2054	M	55	104	1	10	+
70	K2864	M	46	31.5	0	10	+
69	K1126	F	55	94.8	1	10	+
68	K935	M	64	105.2	1	10	+
67	H1034	F	52	99.9	1	9	+
66	K2611	M	51	89.9	0	9	+
65	H90	M	55	122.2	0	9	+
64	K54	M	52	31.7	1	9	+

63	H1533	F	62	111.4	0	9	+
62	H356	M	22	97.2	0	9	+
61	K2014	F	58	94.3	0	9	+
60	K2814	F	65	63.6	0	8	+
59	H2128	M	43	72.1	1	8	+
58	K2032	M	57	78.8	1	8	+
57	K730	M	66	93	1	8	+
56	K1899	F	61	61.4	1	8	+
55	K2130	F	70	81.5	0	8	+
54	K1432	M	43	73.3	0	8	+
53	K1817	M	51	40.2		-	-
52	K155	F	78	113.6	1	-	-
51	K2108	F	69	132.3	0	-	-
50	K1561	F	51	49.3	1	-	-
49	H1979	M	54	119.3	1	-	-
48	K789	F	43	111.4	0	-	-
47	K2420	M	70	105	1	-	-
46	H1254	F	61	113.6	1	-	-
45	H2406	F	50	119.5	0	-	-
44	K1836	F	72	52.4	1	-	-
43	K1805	M	45	50.4	0	-	-
42	K870	F	44	9.5	1	-	-
41	H319	M	62	90	0	-	-
40	H1224	M	54	94.8	1	-	-
39	K2994	M	61	80.3	0	-	-
38	K100	F	36	92.9	0	-	-
37	H298	F	71	121	0	-	-
36	K1837	M	35	63.2	0	-	-
35	K1858	F	65	79.4	0	-	-
34	H1327	M	56	88.4	1	-	-
33	K108	M	50	122	1	-	-
32	K2250	F	60	75.6	0	-	-
31	K1825	F	39	110.5	1	-	-
30	H687	F	76	28.9	1	-	-
29	H1436	F	44	22.5	0	-	-
28	H85	F	40	11.3	1	-	-
27	K2504	F	72		1	-	-
26	K2093	M	64	117.6	0	-	-
25	K1326	M	57	96.5	0	-	-
24	H1592	F	51	66.8	0	-	-
23	K1806	M	72	109.4	1	-	-
22	K1611	F	64	15.3	1	-	-
21	K831	F	54	130.9	0	-	-
20	K877	F	42	7.6	1	-	-

19	K976	F	32	71	1	-	-
18	K2087	M	48	127.7	0	-	-
17	H196	F	64	105.9	1	-	-
16	H2588	F	27	125.4	0	-	-
15	H107	M	46	119.1	1	-	-
14	H119	M	46	83.2	0	-	-
13	K865	F	62	108.6	0	-	-
12	H914	F	59	80.8	0	-	-
11	H921	M	54	58.8	1	-	-
10	H965	F	54	7.4	1	-	-
9	K1082	F	55	49.1	0	-	-
8	H1281	M	36	18.9	1	-	-
7	H1641	M	69	61.9	0	-	-
6	H1871	M	48	117.8	1	-	-
5	K1993	M	72	16.9	0	-	-
4	H2008	M	62	110.2	1	-	-
3	K2059	F	41	90.8	1	-	-
2	K2587	M	59	91.9	0	-	-
1	K2906	M	63	100.7	1	-	-

Table S1C related to **Figure S1** and **Figure 3.**

Characteristics of *H. pylori* ELISA-positive patients from Sumy Regional Clinical Hospital, Ukraine.

The serum samples are displayed according to IT50s tested with *H. pylori* strain 17875/Leb. In addition, *H. pylori* strain J166 identified the series of IT50 titers as positive (+) or negative (–). The location for the background level (the start of the positive IT50 sample is indicated by the horizontal bar) was calibrated with sera from ELISA-negative individuals using *H. pylori* J166.

#	Serum Code	IT50	
		17875/Leb	J166
79	UA-96	1159	+
78	UA-24	1023	+
77	UA-2	476	+
76	UA-84	455	+
75	UA-104	232	+
74	UA-80	232	+
73	UA-82	203	+
72	UA-78	165	+
71	UA-83	160	+
70	UA-39	135	+
69	UA-9	130	+
68	UA-31	130	+
67	UA-16	125	+
66	UA-23	118	+
65	UA-13	116	+
64	UA-98	113	+
63	UA-11	112	+
62	UA-38	108	+
61	UA-66	107	+
60	UA-40	79	+
59	UA-42	78	+
58	UA-6	71	+
57	UA-86	69	+
56	UA-88	69	+
55	UA-8	63	+
54	UA-62	61	+
53	UA-75	57	+
52	UA-21	48	+
51	UA-15	46	+
50	UA-77	38	+
49	UA-10	27	+
48	UA-43	23	+
47	UA-25	20	+
46	UA-79	19	+
45	UA-60	19	+

44	UA-72	17	+
43	UA-46	16	+
42	UA-41	14	+
41	UA-44	12	+
40	UA-100	12	+
39	UA-63	11	+
38	UA-70	10	+
37	UA-52	8	+
36	UA-12	5	+
35	UA-32	-	-
34	UA-14	-	-
33	UA-97	-	-
32	UA-50	-	-
31	UA-59	-	-
30	UA-36	-	-
29	UA-17	-	-
28	UA-89	-	-
27	UA-65	-	-
26	UA-49	-	-
25	UA-76	-	-
24	UA-54	-	-
23	UA-7	-	-
22	UA-20	-	-
21	UA-73	-	-
20	UA-53	-	-
19	UA-74	-	-
18	UA-22	-	-
17	UA-105	-	-
16	UA-57	-	-
15	UA-27	-	-
14	UA-35	-	-
13	UA-5	-	-
12	UA-26	-	-
11	UA-34	-	-
10	UA-55	-	-
9	UA-90	-	-
8	UA-94	-	-
7	UA-30	-	-
6	UA-103	-	-
5	UA-28	-	-
4	UA-92	-	-
3	UA-95	-	-
2	UA-61	-	-
1	UA-91	-	-

Table S1D related to **Figure S1** and **Figure 3.**
Characteristics of *H. pylori* ELISA-positive patients from Baylor College of Medicine, Houston, TX, USA.

The serum samples are displayed according to IT50s tested with *H. pylori* strain 17875/Leb. In addition, *H. pylori* strain J166 identified the series of IT50 titers as positive (+) or negative (–). The location for the background level (the start of the positive IT50 sample is indicated by the horizontal bar) was calibrated with sera from ELISA-negative individuals using *H. pylori* J166.

#	Serum Code	IT50	
		17875/Leb	J166
141	11352	794	+
140	11377 A	350	+
139	12478	312	+
138	11360	289	+
137	12121 A	274	+
136	12150 A	268	+
135	12364	252	+
134	12490	242	+
133	11526	221	+
132	11883 B	171	+
131	11358 B	156	+
130	11263	146	+
129	13182	145	+
128	12866	131	+
127	11361	111	+
126	12838	109	+
125	11538	105	+
124	12381	105	+
123	12424	104	+
122	13192	96	+
121	12609	96	+
120	11327	93	+
119	12804	87	+
118	12854	84	+
117	13178	82	+
116	13185	81	+
115	11240	80	+
114	13789	79	+
113	12562	75	+
112	12815	75	+
111	12456	63	+
110	12643	60	+
109	11369 A	58	+

108	11326	57	+
107	11344 A	55	+
106	12342	53	+
105	12798	52	+
104	11485 B	50	+
103	11843 A	47	+
102	12853	44	+
101	12502	44	+
100	11255	39	+
99	12343	39	+
98	12292	39	+
97	11613	36	+
96	12803	36	+
95	11252	33	+
94	12868	31	+
93	12922	29	+
92	12533	28	+
91	12970	27	+
90	11281	26	+
89	12614	25	+
88	12786	24	+
87	13067	24	+
86	12341	24	+
85	11355	23	+
84	12544	23	+
83	11332	22	+
82	11248	21	+
81	11465 B	20	+
80	11376 A	20	+
79	11677 A	19	+
78	11325	19	+
77	11443 A	18	+
76	13175	17	+
75	12351	17	+
74	13714 A	16	+
73	12812	15	+
72	13003	14	+
71	11333 B	14	+
70	12968	14	+
69	12344	13	+
68	12886	13	+
67	11266	12	+
66	12188	11	+
65	11842 A	11	+
64	11834 A	10	+

63	11837 A	9	+
62	12430	9	+
61	11891 A	9	+
60	12817	8	+
59	11353 B	8	+
58	11829 A	-	-
57	11660	-	-
56	12830	-	-
55	11320	-	-
54	11351 A	-	-
53	11354	-	-
52	12869	-	-
51	12566	-	-
50	11884 A	-	-
49	12753	-	-
48	11258	-	-
47	12800	-	-
46	13179	-	-
45	12126 A	-	-
44	11364	-	-
43	12795	-	-
42	15395 A	-	-
41	13191	-	-
40	11631 B	-	-
39	12399	-	-
38	12159 B	-	-
37	12345	-	-
36	11882 A	-	-
35	11888 A	-	-
34	11813 A	-	-
33	11874 A	-	-
32	11444 A	-	-
31	11445 A	-	-
30	11371 A	-	-
29	11367 B	-	-
28	11368 B	-	-
27	11260	-	-
26	11348 A	-	-
25	11343 A	-	-
24	1340 A	-	-
23	11258	-	-
22	1335 C	-	-
21	11349 A	-	-
20	13172	-	-

19	13173	-	1-
18	13174	-	-
17	13184	-	-
16	12876	-	-
15	12906	-	-
14	13177	-	-
13	13181	-	-
12	12858	-	-
11	12910	-	-
10	12837	-	-
9	13791	-	-
8	12611	-	-
7	11289	-	-
6	11888 B	-	-
5	11352	-	-
4	11335 d	-	-
3	11635 C	-	-
2	12339	-	-
1	12368	-	-

2
3

Table S1E related to **Figure S1** and **Figure 3.**
Characteristics of *H. pylori* ELISA-positive patients from Mexico UMAE Pediatria, Mexico City, Mexico.

The serum samples are displayed according to IT50s tested with *H. pylori* strain 17875/Leb. In addition, *H. pylori* strain J166 identified the series of IT50 titers as positive (+) or negative (–). The location for the background level (the start of the positive IT50 sample is indicated by the horizontal bar) was calibrated with sera from ELISA-negative individuals using *H. pylori* J166.

#	Serum Code	IT50	
		17875/Leb	J166
200	326	1651	+
199	261	799	+
198	150	581	+
197	426	561	+
196	15	552	+
195	151	513	+
194	10	488	+
193	5	451	+
192	24	413	+
191	51	378	+
190	119	374	+
189	227	338	+
188	300	313	+
187	188	302	+
186	220	300	+
185	13	287	+
184	431	274	+
183	57	256	+
182	174	247	+
181	336	228	+
180	422	214	+
179	535	203	+
178	56	193	+
177	182	191	+
176	263	190	+
175	530	171	+
174	372	168	+
173	37	151	+
172	250	151	+
171	297	148	+
170	125	148	+
169	59	137	+
168	395	136	+

167	353	131	+
166	140	125	+
165	451	122	+
164	278	120	+
163	264	115	+
162	158	115	+
161	175	114	+
160	106	113	+
159	2	108	+
158	21	107	+
157	553	107	+
156	23	105	+
155	401	104	+
154	468	100	+
153	444	95	+
152	456	92	+
151	204	91	+
150	11	82	+
149	228	77	+
148	591	74	+
147	27	74	+
146	31	73	+
145	235	71	+
144	407	67	+
143	14	66	+
142	434	66	+
141	344	66	+
140	543	65	+
139	531	62	+
138	539	62	+
137	130	60	+
136	552	59	+
135	9	57	+
134	145	57	+
133	371	56	+
132	237	54	+
131	6	54	+
130	284	52	+
129	615	51	+
128	134	50	+
127	43	49	+
126	36	49	+
125	29	49	+
124	576	48	+
123	593	47	+

122	419	45	+
121	437	42	+
120	44	40	+
119	206	38	+
118	608	37	+
117	339	37	+
116	574	36	+
115	415	36	+
114	219	36	+
113	541	35	+
112	379	32	+
111	449	31	+
110	32	31	+
109	238	31	+
108	41	30	+
107	421	30	+
106	521	29	+
105	397	29	+
104	240	29	+
103	208	28	+
102	439	27	+
101	454	27	+
100	194	27	+
99	193	26	+
98	184	25	+
97	54	25	+
96	393	25	+
95	40	24	+
94	296	24	+
93	469	24	+
92	400	23	+
91	467	22	+
90	257	21	+
89	77	21	+
88	465	21	+
87	442	20	+
86	241	20	+
85	355	20	+
84	446	20	+
83	52	20	+
82	579	19	+
81	95	19	+
80	211	19	+
79	558	18	+
78	259	18	+

77	580	18	+
76	271	18	+
75	50	17	+
74	403	17	+
73	181	17	+
72	45	16	+
71	63	16	+
70	239	16	+
69	3	16	+
68	409	15	+
67	177	15	+
66	131	14	+
65	248	14	+
64	440	14	+
63	112	13	+
62	331	13	+
61	390	13	+
60	550	13	+
59	33	12	+
58	163	12	+
57	582	-	-
56	35	-	-
55	528	-	-
54	286	-	-
53	7	-	-
52	602	-	-
51	49	-	-
50	78	-	-
49	26	-	-
48	450	-	-
47	38	-	-
46	542	-	-
45	162	-	-
44	525	-	-
43	522	-	-
42	122	-	-
41	34	-	-
40	387	-	-
39	267	-	-
38	55	-	-
37	62	-	-
36	466	-	-
35	48	-	-
34	583	-	-

33	53	-	-
32	66	-	-
31	159	-	-
30	600	-	-
29	25	-	-
28	599	-	-
27	30	-	-
26	545	-	-
25	39	-	-
24	47	-	-
23	554	-	-
22	592	-	-
21	58	-	-
20	544	-	-
19	20	-	-
18	609	-	-
17	399	-	-
16	8	-	-
15	17	-	-
14	60	-	-
13	294	-	-
12	4	-	-
11	12	-	-
10	18	-	-
9	19	-	-
8	22	-	-
7	28	-	-
6	129	-	-
5	142	-	-
4	144	-	-
3	270	-	-
2	327	-	-
1	380	-	-

Table S1F related to **Figure 1.**
Characteristics of *H. pylori* ELISA-positive patients from Regional Children Hospital and St. Zinaida City Children Hospital, Sumy, Ukraine.

#	Serum Code	Age	IT50 17875/Leb
36	UA-206	9	7100
35	UA-327	15	717
34	UA-292	17	546
33	UA-308	17	338
32	UA-238	15	253
31	UA-266	5	243
30	UA-236	15	208
29	UA-280	9	141
28	UA-247	14	120
27	UA-307	9	86
26	UA-319	14	75
25	UA-318	7	74
24	UA-290	9	51
23	UA-223	7	50
22	UA-331	13	24
21	UA-310	11	15
20	UA-303	14	8
19	UA-203	7	-
18	UA-205	4	-
17	UA-220	3	-
16	UA-243	15	-
15	UA-245	16	-
14	UA-276	7	-
13	UA-289	9	-
12	UA-296	17	-
11	UA-305	15	-
10	UA-306	17	-
9	UA-309	13	-
8	UA-311	8	-
7	UA-316	13	-
6	UA-321	13	-
5	UA-322	15	-
4	UA-324	16	-
3	UA-328	17	-
2	UA-332	17	-
1	UA-335	17	-

Table S2A related to **Figure 3A.**
Leb-binding affinities of Swedish strains.

Diagnosis	Strain	Ka Leb
Gastritis	Sw62	-[a]
	Sw3	-[a]
	Sw10	-[a]
	Sw11	-[a]
	Sw15	-[a]
	Sw29	-[a]
	Sw56	-[a]
	Sw57	-[a]
	Sw67	-[a]
	Sw69	-[a]
	Sw125	-[a]
	Sw58	-[a]
	Sw70	-[a]
	Sw77	-[a]
	Sw79	-[a]
	Sw80	-[a]
	Sw86	-[a]
	Sw123	-[a]
	Sw82	-[a]
	Sw84	6.84E+08
	Sw114	9.37E+08
	Sw76	1.00E+09
	Sw59	1.04E+09
	Sw72	1.55E+09
	Sw116	1.65E+09
	Sw60	2.41E+09
	Sw47	2.72E+09
	Sw78	3.05E+09
	Sw65	3.09E+09
	Sw75	3.19E+09
	Sw119	4.09E+09
	Sw117	4.35E+09

	Sw81	7.38E+09
	Sw42	1.22E+10
	Sw115	2.23E+10
	Sw87	2.25E+10
	Sw66	2.63E+10
	Sw4	2.74E+10
	Sw68	3.04E+10
	Sw89	4.11E+10
	Sw61	5.44E+10
	Sw126	5.84E+10
	Sw27	6.54E+10
	Sw127	6.57E+10
	Sw64	8.41E+10
	Sw63	1.75E+11
DU	Sw1	-[a]
	Sw20	-[a]
	Sw52	-[a]
	Sw31	-[a]
	Sw50	2.18E+08
	Sw13	4.47E+09
	Sw24	9.17E+09
	Sw51	1.04E+10
	Sw39	1.55E+10
	Sw30	2.32E+10
	Sw45	3.04E+10
	Sw54	3.14E+10
	Sw43	3.23E+10
	Sw18	4.92E+10
	Sw7	5.44E+10
	Sw38	9.21E+10
	Sw44	1.04E+11
	Sw53	1.58E+11
	Sw5	1.66E+11

-[a] Ka data are missing because the strain does not produce detecTable Leb binding.
Leb binding affinities of Swedish *H. pylori* strains are described in [11].

Table S2B related to **Figure S1G (Leb-Cocktail)** and **Figure S3A (Leb-Hot).**

Leb-binding properties of Mexican strains and corresponding serum IT50s.

Diagnosis	Strain	Leb-Hot, %	Leb-Cocktail, %	Serum Code	Serum IT50
Gastritis	Mc1201	19	8	386	1
	Mc1205	77	1	203	1
	Mc1207	30	10	21	116
	Mc1215	41	3	171	70
	Mc1216	76	29	110	1
	Mc1217	84	24	68	39
	Mc1218	82	12	79	59
	Mc1219	5	2	31	16
	Mc1221	52	20	345	64
	Mc1222	0	0	12	1
	Mc1223	0	0	22	ND[a]
	Mc1227	80	41	75	4
	Mc1229	3	1	217	107
	Mc1230	1	0	566	92
	Mc1231	69	29	68	39
	Mc1236	80	21	747	ND[a]
DU	Mc1202	84	18	419	50
	Mc1203	47	2	1045	1
	Mc1204	86	31	902	89
	Mc1206	30	1	1040	7
	Mc1208	63	28	415	43
	Mc1209	74	40	798	98
	Mc1210	86	53	465	27
	Mc1211	86	67	979	84
	Mc1212	47	2	899	1
	Mc1213	85	24	1075	28
	Mc1214	70	34	1038	118
	Mc1220	63	24	70	46
	Mc1224	1	0.5	918	1
	Mc1225	1	0.3	1070	1
	Mc1226	1	0.5	1085	127
	Mc1228	72	17	372	193

ND[a] - IT50 is **N**ot **D**efined (**LOW**)

Table S3 related to **Figure 3** and **Figure S3**.
Sera IT50 from Non-Atrophic Gastritis (NAG) and Duodenal Ulcer disease (DU) patients.

Serum Code	Diagnosis	ELISA *H. pylori*	IT50 by different test-strains							no. of blue boxes
			17875/Leb	Mc1204	J166	Mc1207	Mc1215	Sw44	I9	
201-14	NAG	3.5	34	69	234	386	103	75	127	5
201-84	NAG	2.1	208	118	424	509	344	1419	381	5
201-99	NAG	1.9	46	33	64	96	49	73	75	5
201-113	NAG	6.0	1	5	31	37	26	1		0
201-118	NAG	3.3	31	14	40	52	43	8	8	2
201-137	NAG	10.8	135	151	555	1494	482	180		5
201-143	NAG	2.2	38	35	266	178	12	51		4
201-352	NAG	7.2	1	1	1	43	15	1	8	0
201-406	NAG	12.8	44	590	2285	1221	413	721		5
201-464	NAG	2.7	34	80	351	399	155	78		5
201-526	NAG	1.2	1	17	91	473	90	7		5
201-537	NAG	1.0	1	12	35	58	27	1	32	1
201-540	NAG	2.1	1	6	44	46	10	1	1	0
201-560	NAG	5.1	37	51	73	160	218	25		5
201-568	NAG	7.8	34	68	441	1203	197	86		5
5	NAG	5.2	282	106	198	1515	733	343		5
10	NAG	9.8	1	2	27	27	42	1	9	1
12	NAG	1.2	1	22	8	23	8	1	5	0
15	NAG	3.3	337	794	2019	541	998	294		5
21	NAG	7.8	116	143	501	916	291	153		5
31	NAG	4.0	16	15	70	171	62	56		5
51	NAG	3.8	277	93	680	1015	662	264		5
68	NAG	5.7	39	51	267	214	39	34		5
75	NAG	1.7	4	7	13	355	11	12	77	3
79	NAG	1.0	59	74	243	637	246	71		5
110	NAG	0.9	1	2	12	12	8	1	3	0
146	NAG	1.5	2	16	85	72	15	1	14	2
160	NAG	6.5	82	54	310	355	365	232		5
171	NAG	1.2	70	264	1106	742	203	298		5

176	**NAG**	2.8	25	20	430	71	132	69	65	**5**
203	**NAG**	5.5	1	4	60	13	1	1	4	**1**
217	**NAG**	4.8	107	45	839	794	230	29		**5**
345	**NAG**	3.7	64	43	142	602	252	1		**4**
386	**NAG**	4.4	1	9	107	147	41	1	57	**4**
566	**NAG**	1.3	92	204 1	3167	145	230	189		**5**
372	**DU**	9.6	193	416	2139	543	324	115		**5**
70	**DU**	3.9	46	33	407	348	106	98		**5**
415	**DU**	4.6	43	51	358	303	391	36		**5**
419	**DU**	4.4	50	144	1263	54	55	37	224	**5**
439	**DU**	9.4	28	94	507	217	357	104		**5**
465	**DU**	11.1	27	112	400	210	55	28		**5**
522	**DU**	0.7	1	3	26	36	21	1	7	**0**
767	**DU**	2.1	22	10	71	62	17	1	35	**3**
776	**DU**	4.1	1	1	45	24	22	1	1	**0**
790	**DU**	3.8	102	19	145	1193	212	482		**5**
798	**DU**	1.0	98	84	589	527	208	177		**5**
899	**DU**	0.4	1	1	18	23	14	1	33	**0**
902	**DU**	0.5	89	499	1021	651	534	202		**5**
903	**DU**	0.5	1	5	107	50	1	1	29	**3**
904	**DU**	0.7	1	4	38	63	9	1	20	**1**
906	**DU**	0.6	1	4	43	33	19	1	6	**0**
913	**DU**	0.6	1	2	25	30	45	1	8	**1**
918	**DU**	1.3	1	9	99	89	12	7	53	**4**
919	**DU**	1.0	28	43	921	365	46	93		**5**
920	**DU**	1.3	1	1	13	17	27	1		**0**
921	**DU**	9.6	47	26	299	319	57	62		**5**
938	**DU**	0.3	1	217	415	514	61	167		**5**
958	**DU**	2.4	5	15	141	224	1	16		**4**
960	**DU**	3.7	31	14	39	182	24	29		**3**
979	**DU**	6.7	84	8	186	90	176	25	98	**5**
983	**DU**	0.5	1	1	9	28	16	1	10	**0**
994	**DU**	0.6	45	42	388	1163	261	119		**5**
995	**DU**	4.3	1	15	60	65	34	17	34	**5**
1008	**DU**	0.8	27	41	167	50	128	59	98	**5**
1010	**DU**	6.4	1	7	130	36	52	1	3	**3**
1019	**DU**	1.3	1	3	62	64	32	1	29	**3**
1034	**DU**	1.6	1	1	12	20	33	1	1	**1**

1038	**DU**	1.2	118	114	186	646	242	256		**5**
1040	**DU**	1.3	7	30	160	113	93	1	84	**4**
1041	**DU**	0.8	4	57	164	56	405	22	265	**5**
1045	**DU**	0.5	1	2	56	104	45	1	13	**4**
1062	**DU**	3.0	231	348	882	631	367	322		**5**
1066	**DU**	1.0	1	7	35	58	19	7	23	**2**
1069	**DU**	2.1	1	1	11	42	8	1	7	**0**
1070	**DU**	2.3	1	12	338	44	22	1	61	**2**
1074	**DU**	2.0	1	14	165	55	34	1	55	**4**
1075	**DU**	3.3	28	178	569	255	91	190		**5**
1085	**DU**	3.8	127	353	479	1031	368	64		**5**
1086	**DU**	1.3	1	4	7	26	28	1	4	**0**
			Positive IT50:		**50**	**50**	**28**	**2**	**33**	

Explanation for the column “No. of (blue) boxes)”. The IT50 titers for 17875/Leb and Mc1204 are considered positive if two or more of the five reporter strains (**J166, Mc1207, Mc1215, Sw 44**, and **I9)** are positive (indicated by blue color) for IT50. If only a single reporter strain is positive and the rest are negative (yellow) or all reporter strains are negative (yellow), the serum is considered negative for IT50 and is not included in the Odds Ratio calculations. Those sera are indicated with a full yellow stripe.

There are 8 sera samples that are IT50 negative in the NAG cluster, compared to 11 IT50-negative sera samples in the DU cluster, which corresponds to 23% and 25%, respectively.

In the 17875/Leb column and the Mc1204 column, the sera that demonstrate IT50 <30 are colored red (LOW), whereas the sera samples with IT50 >30 are colored green (HIGH). The IT50 = 30 critical value was defined from the comparison of all possible odds ratios, see **Figure 3C**.

The ratio between High and Low for the NAG vs. DU sera samples was used to assess the Odds Ratio. There were 21 *vs.* 6 (a 3.5-fold difference) sera samples with IT50 higher *vs.* lower than 30 among NAG patients, compared to 14 *vs.* 19 (a 0.74-fold difference) for DU patients, which generated the Odds Risk as 3.5/0.74 = 4.75 (**Figure 3D*i***).

Table S4 related to **Figure 1** and **Figure S1** and **Figure 3E.**

The locations of the IT50 = 30 interval in the different cohorts were identified by strain 17875/Leb, whereas the locations of IT50 positive *vs*. negative sera in the different cohorts were identified by strain J166.

#1	#2	#3	#4	#5	#6	#7
Serum Series	Number of individual sera samples	Serum no. for the IT50 = 30 interval	Serum no. in the middle of IT50 = 30 interval	Serum samples with IT50 > 30	Sera no. for the IT50 -positive interval	IT50-positive individuals
Kalixanda	322	180 - 189	184	43%	54 - 322	84%
Ukraine	79	52 - 56	54	33%	36 - 79	56%
USA	141	94 - 98	96	33%	59 - 141	59%
Mexico	200	131 - 139	135	33%	58 - 200	72%
Referred to:	**Table S1**	**Figure 3E**	**Figure 3E**	**Figure 3E**	**Table S1**	

Column #1: IT50s were tested by sera samples from four world-wide populations (all data in **Table S1)**
Column #2: The number of individual sera samples from each population.
Column #3: The sera sample numbers corresponding to the IT50 = 30 interval, i.e., IT50 < 30 in samples 1–179 and IT50 > 30 in samples 190–322 in the Kalixanda cohort.
Column #4: The sera sample indicates the mid sample of the IT50 = 30 interval from Column 3.
Column #5: The prevalence of serum samples with IT50 > 30, e.g., samples no. 184–322 out of the 322 samples (43%) in the Kalixanda cohort.
Column #6: The sera samples that are positive for IT50 after testing with the sensitive low-affinity Leb-binding strain J166.
Column #7: The group of individuals (in %) that are IT50 positive (from Column 6).

Table 5 related to **Fig 5** and **Figure S5**
Crystallographic data collection and refinement statistics for the BabA protein co-crystallized with ABbA **(Table 5).**

	BabA^{AD}-Nb19-ABBA
Data collection	
Space group	P 1 2_1 1
Cell dimensions	
a, *b*, *c* (Å)	99.7, 68.4, 176.6
α, β, γ (°)	90.0, 104.4, 90.0
Resolution (Å)	39.45-2.70 (2.77-2.70)*
R_{meas}	6.0 (88.4)*
$I/\sigma I$	15.1 (2.1)*
CC1/2	99.9 (86.4)*
Completeness (%)	99.2 (99.3)*
Redundancy	4.3 (4.5)*
Refinement	
Resolution (Å)	39.5-2.7
No. reflections	63297
R_{work}/ R_{free}	22.9 / 28.3
No. atoms	
Protein	13995
Water	4
B-factors	
Protein	110.6
Water	95.5
R.m.s deviations	
Bond lengths (Å)	0.01
Bond angles (º)	

Table S6A related to **Fig 6** and **fig S6.**
Binding properties and IC50 of Eurasian *H. pylori* strains.
S831, I109, and I119 are marked in red as the Specialists among 49 European and 27 Asian strains.

Origin	#	Strain	Leb-Hot (%)	ABbA-Hot (%)	IC50, nM
Europe	1	**17875/Leb**	92	90	0.1
	2	**J166**	33	1	25
	3	**USU101**	78	12	0.4
Sweden	1	**Sw2**	94	54	0.1
	2	**Sw4**	61	0.2	7
	3	**Sw6**	73	54	0.03
	4	**Sw7**	38	37	0.1
	5	**Sw8**	91	83	0.05
	6	**Sw17**	96	1	6
	7	**Sw19**	76	14	0.4
	8	**Sw21**	93	43	0.2
	9	**Sw27**	95	31	0.7
	10	**Sw38**	82	2	2
	11	**Sw41**	28	22	0.2
	12	**Sw43**	86	57	0.03
	13	**Sw44**	42	54	0.1
	14	**Sw45**	88	29	0.3
	15	**Sw53**	95	80	0.06
	16	**Sw60**	22	42	0.04
	17	**Sw61**	86	53	0.1
	18	**Sw63**	92	64	0.1
	19	**Sw64**	95	54	0.3
	20	**Sw65**	38	43	0.2
	21	**Sw66**	83	34	0.4
	22	**Sw68**	89	31	0.5
	23	**Sw75**	24	0.3	4
	24	**Sw89**	76	28	0.2
	25	**Sw99**	92	40	0.2
	26	**Sw103**	94	53	0.7

	27	**Sw105**	87	68	0.05
	28	**Sw110**	93	56	0.3
	29	**Sw126**	91	51	0.2
Germany	1	**G929**	77	48	0.1
	2	**G932**	89	61	0.1
	3	**G962**	95	73	0.3
	4	**G965**	95	65	0.2
Spain	1	**S808**	78	8	0.7
	2	**S819**	94	55	0.3
	3	**S828**	41	55	0.04
	4	**S830**	95	54	0.3
	5	**S831**	54	1	>100
	6	**S845**	44	2	4
	7	**S847**	88	33	0.6
	8	**S851**	63	32	0.5
	9	**S855**	92	50	0.2
	10	**S860**	95	43	0.5
	11	**S863**	97	53	0.3
	12	**S864**	91	35	0.4
	13	**S865**	97	43	0.7
India	1	**I99**	23	2	1.6
	2	**I93**	74	2	>100
	3	**I9**	74	38	0.38
	4	**I78**	30	2	12
	5	**I60**	81	5	4
	6	**I21**	87	2	>100
	7	**I18**	92	39	0.3
	8	**I17**	74	2	6
	9	**I120**	75	29	1
	10	**I110**	94	28	0.1
	11	**I109**	75	2	4
	12	**I102**	17	1	>100
	13	**I119**	52	10	0.3
China	1	**Ch1**	97	78	0.3

Japan	1	**J503**	96	46	1
	2	**J506**	11	1	>100
	3	**J507**	94	2	>100
	4	**J509**	92	29	0.9
	5	**J511**	36	55	0.06
	6	**J512**	35	54	0.06
	7	**J513**	96	4	72
	8	**J517**	94	26	0.89
	9	**J519**	87	62	0.04
	10	**J520**	90	18	5
	11	**J531**	92	2	15
	12	**J532**	95	42	0.5
	13	**J533**	94	66	0.08

Binding properties and IC50s of Eurasian *H. pylori* strains.
S831, I109, and I119 are marked in red as the Specialists
among 49 European and 27 Asian strains.

Table S6B related to **Fig 6** and **fig S6.**
Binding properties and preferences and IC50s of North and South Indigenous American and Latin-American *H. pylori* strains.
Leb-H, % - binding to **H**ot HSA-Leb conjugate
Leb-C, % - binding to **C**ocktail-HSA-Leb conjugate
ALeb-C, % - binding to **C**ocktail-HSA-ALeb conjugate
ND - Not Determined
O - Specialists are the strains with a >2.5 ratio in Leb/ALeb binding [11].
A - Specialists are the strains with a <0.4 ratio in Leb/ALeb binding [11].

Origin	#	Strain	Leb-H (%)	Leb-C (%)	ALeb-C (%)	ABO Preference	ABbA-Hot (%)	IC50, nM
Alaska / North America	1	**A702**	97	37	26	Generalist	41	1
	2	**A703**	94	32	32	Generalist	45	0.5
	3	**A710**	91	36	38	Generalist	0.3	>100
	4	**A712**	54	16	13	Generalist	4	0.7
	5	**A713**	24	6	2	O-Specialist	6	0.7
	6	**A714**	96	23	21	Generalist	82	0.2
	7	**A718**	16	0	16	A-Specialist	0.5	>100
	8	**A723**	70	11	0	O-Specialist	0.3	>100
	9	**A730**	26	6	19	A-Specialist	19	0.3
	10	**A733**	64	46	37	Generalist	1	30
	11	**A736**	94	34	30	Generalist	0.7	>100
Mexico, Latin America	1	**Mc 1201**	22	12	0	O-Specialist	0.3	>100
	2	**Mc 1202**	95	15	12	Generalist	0.4	>100
	3	**Mc 1203**	53	2	2	Generalist	21	0.2
	4	**Mc 1204**	97	38	33	Generalist	3	2
	5	**Mc 1205**	87	3	0	O-Specialist	0.5	>100
	6	**Mc 1206**	34	2	2	Generalist	18	0.3
	7	**Mc 1207**	34	ND*	ND	ND	2	2
	8	**Mc 1208**	71	12	7	Generalist	25	>100
	9	**Mc 1209**	84	40	0	O-Specialist	1	>100
	10	**Mc 1210**	97	39	34	Generalist	4	6
	11	**Mc 1211**	97	ND	ND	ND	5	6
	12	**Mc 1212**	53	3	3	Generalist	23	0.3
	13	**Mc 1213**	95	28	3	O-Specialist	25	1
	14	**Mc 1214**	79	29	9	O-Specialist	1	3

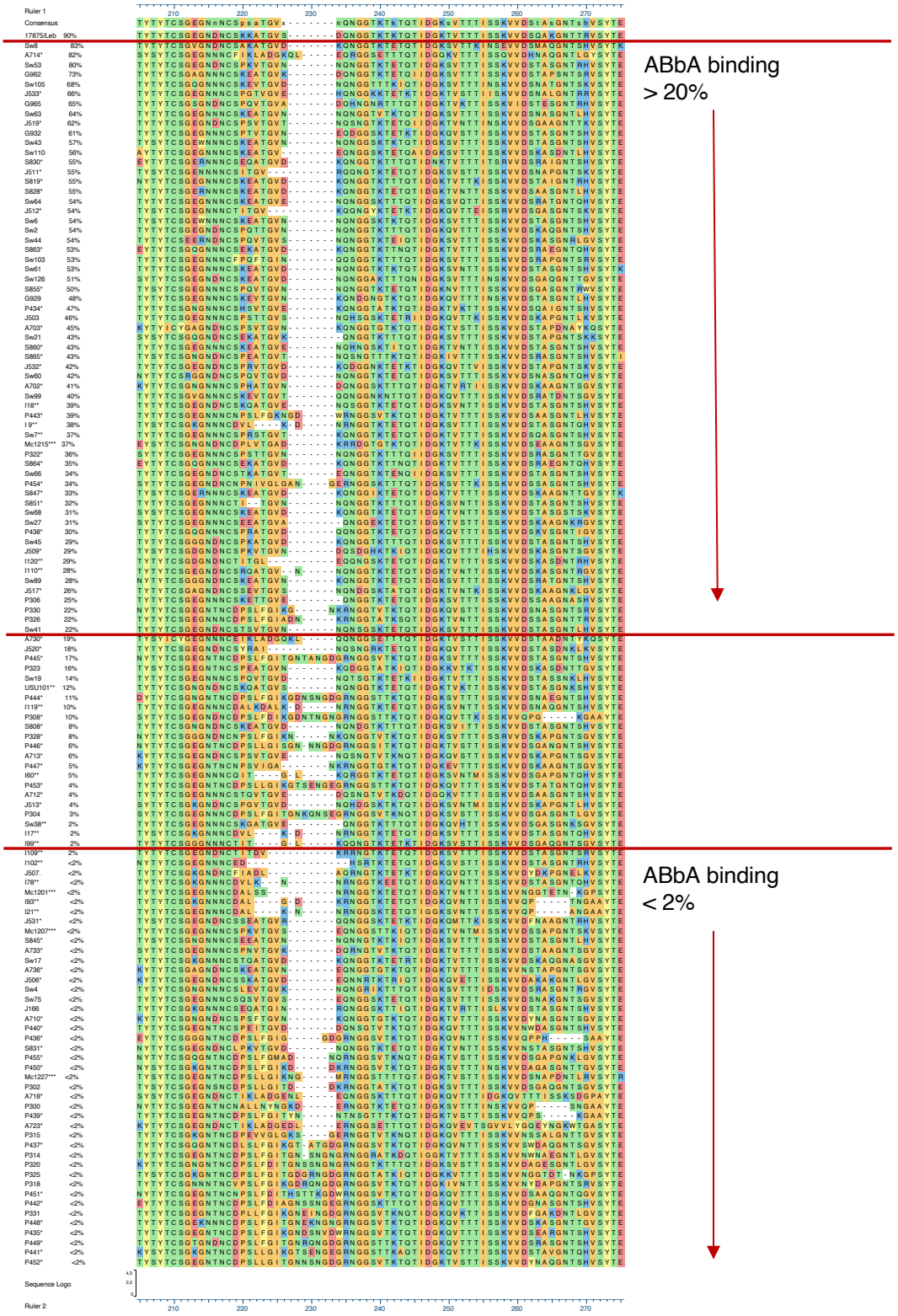
	15	**Mc 1215**	46	2	1	Generalist	37	0.08
	16	**Mc 1216**	86	24	22	Generalist	1	5
	17	**Mc 1217**	95	16	1	O-Specialist	0.9	>100
	18	**Mc 1218**	92	16	5	O-Specialist	0.9	>100
	19	**Mc 1219**	6	2	0	O-Specialist	0.9	>100
	20	**Mc 1220**	71	ND	ND	ND	0.7	>100
	21	**Mc 1221**	58	ND	ND	ND	0.5	>100
	22	**Mc 1227**	80	42	0	O-Specialist	1.3	5
Peru, South America	1	**P300**	91	23	0	O-Specialist	0.4	>100
	2	**P302**	80	26	0	O-Specialist	0.5	43
	3	**P304**	61	14	0	O-Specialist	2.7	1
	4	**P306**	92	70	59	Generalist	25	0.2
	5	**P308**	94	31	4	O-Specialist	10	47
	6	**P314**	94	40	5	O-Specialist	0.8	>100
	7	**P315**	74	18	0	O-Specialist	0.7	>100
	8	**P318**	97	53	0	O-Specialist	0.8	>100
	9	**P320**	65	28	0	O-Specialist	1.2	>100
	10	**P322**	98	46	36	Generalist	36	0.2
	11	**P323**	43	20	11	Generalist	16	0.4
	12	**P325**	88	16	1	O-Specialist	0.8	>100
	13	**P326**	94	22	2	O-Specialist	22	0.2
	14	**P328**	91	38	34	Generalist	8	2
	15	**P330**	95	28	0	O-Specialist	22	0.5
	16	**P331**	93	31	0	O-Specialist	0.4	>100
	17	**P434**	92	40	31	Generalist	47	0.1
	18	**P435**	40	16	0	O-Specialist	1.6	7
	19	**P436**	93	49	12	O-Specialist	0.7	>100
	20	**P437**	81	15	8	Generalist	0.7	>100
	21	**P438**	72	19	7	O-Specialist	30	0.9
	22	**P439**	14	2	14	A-Specialist	0.3	>100
	23	**P440**	58	32	25	Generalist	0.3	>100
	24	**P441**	88	42	3	O-Specialist	0.9	>100
	25	**P442**	96	46	5	O-Specialist	0.5	>100
	26	**P443**	61	12	0	O-Specialist	39	0.2

	27	**P444**	62	21	0	O-Specialist	11	0.6
	28	**P445**	95	34	0	O-Specialist	17	1
	29	**P446**	32	16	0	O-Specialist	6	1
	30	**P447**	69	33	1	O-Specialist	5	3
	31	**P448**	71	31	0	O-Specialist	0.1	>100
	32	**P449**	96	62	17	O-Specialist	0.3	3
	33	**P450**	47	12	0	O-Specialist	0.3	>100
	34	**P451**	12	8	0	O-Specialist	0.7	>100
	35	**P452**	80	25	1	O-Specialist	0.1	>100
	36	**P453**	93	56	3	O-Specialist	4	8
	37	**P454**	78	27	0	O-Specialist	34	0.4
	38	**P455**	92	27	0	O-Specialist	1.5	3

1
2

Table S7 related to **Fig 6** and **fig S6.**

BabA alignment (aa185-247) according to ABbA binding strength.



Sequences that originated from (11) are indicated by one star *.
Sequences that originated from (14) are indicated by two stars **.
Mexican Mc1201, Mc1207, Mc1215 and Mc1227 are indicated by three stars ***
and were sequenced by the J. Torres lab (co-author).

Table S8 related to **Figure 6** and **Figure S6.**
ABbA binding properties of global *H. pylori* strains and of Generalist *vs*. Specialist *H. pylori* strains.

Table S8A (Figure 6A)

ABbA binding (%)	European	Asian	Americas
RIA, >20%	57.4	19.1	23.5
RIA, <2%	11.5	13.5	75

Table S8B (Figure 6B)

ABbA binding (%)	Generalists	Specialists
RIA, >20%	91.2	8.8
RIA, <2%	38.8	61.2

Table S8C (Figure 6C)

ABbA binding (%)	Specialists
RIA, >20%	37.5
RIA, <2%	80.6

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