

## Forum

# The Global Synanthrome Project: A Call for an Exhaustive Study of Human Associates

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**Here we coin the term synanthrome to describe all of the species we interact with. We propose that the time is now here for The Global Synanthrome Project to describe all of our interacting species and how they have changed through time and across space. This effort must involve natural history, ecology, and evolutionary biology in addition to genomics studies that are already underway.**

As much as any individual scholar, Mary-Claire King changed how we think about what it means to be human. She did so using genetics as a lens through which to see what was otherwise invisible. In her hands this lens offered many insights. It was King who first identified a key locus on 17q21 associated with early-onset breast cancer. It would also be King who, in 1975, first compared the genetic similarity of humans and chimpanzees [1]. It was known that chimpanzees and humans are kin, but just how similar are they? One could only really guess. Yet it seemed clear that many differences between chimpanzees and humans demanded explanation: one species is a hunched knuckle-walker, the other walks upright; one is covered with hair, the other seemingly hairless; one is able to build cities, write, read, and make music, while the other one cannot.

King compared the amino acid sequences of genes of chimpanzees and humans and

discovered that they were not 50% similar genetically, or 60%, or even 80%, but instead nearly identical, with 99% identity [1]. All of the differences between them and us must relate to this tiny sliver of genetic difference, or at least that is how it seemed at the time.

What has followed has been a rich and detailed consideration, a consideration that is still very much underway, of the modest DNA sequence difference between humans and chimpanzees. We now know many of the genes that lead human and chimpanzee immune systems to be so different, and we have some suspicion as to which genes are associated with why chimpanzees never get the kind of heart attack we get [2].

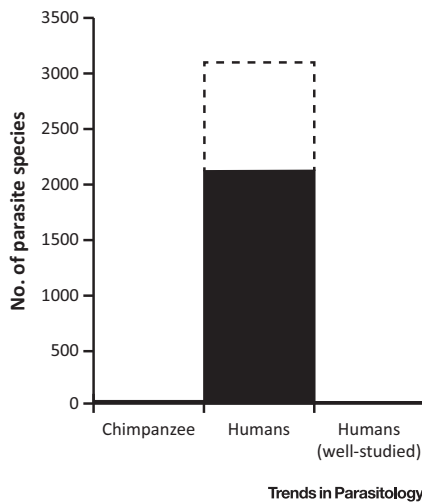
Amidst all these important studies, a critically important difference has been largely ignored. While geneticists were comparing humans and chimpanzees, parasitologists were doing something very different. They were carefully compiling lists of the parasites that live in or on chimpanzees and humans (and any other species they could get their hands on, for that matter). For parasitologists, these included both big things (such as worms and mites), little things (such as protists), and truly tiny things like viruses. But they faced a barrier to progress. The parasitologists studying humans and those studying chimpanzees and other nonhuman primates were not talking very much [3]. Thus, while each group had a tally of the organisms found in their study animals, the tallies were not often compared. But such a comparison is important. A large proportion of the genes (and their products, including proteins) of any organism are those of its parasites and pathogens. Someone who is infected by many worm species, for instance, may actually be dragging around more worm genes than human genes! We are what eats in us.

When we pulled together the lists of pathogens and parasites of chimpanzees [4] and a list of those of humans ([5] pooled

with [6]), we were in for a surprise like that of Mary-Claire King, but the difference was unexpectedly huge rather than tiny (Figure 1). Humans have been found to be hosts for 2107 parasites and pathogens to date, and just a handful of these, fewer than 30, have ever been documented in chimpanzees. We have many of the same parasites and pathogens as them (though far less than 99%) but they lack nearly all of those found in us [7]. From the perspective of the genes of parasites and pathogens, humans and chimpanzees are wildly different.

How did this happen? As population sizes of humans increased, exposure to, and infection by, parasites and pathogens of other primates increased [7]. Then, as humans became more sedentary and began to domesticate and then associate with agricultural species, we picked up pathogens found in those species. Each place we moved, we picked up more new pathogens from new interactions. Rabbits, lions, cows, and pigs have all donated to us some of what ailed them. With these new ecological interactions, a whole new group of pathogens evolved that depended on large and dense populations (cold viruses for instance [8]). As a result, humans and chimpanzees are no longer that similar. The differences in the species we associate with – our parasites and pathogens – are the biggest differences between our closest living relatives and us.

But there is more. What we have discussed so far are the collective differences, all of the species found in chimpanzees compared to all of those found in humans. The story is different for the comparison of an individual chimpanzee and an individual human. Here, the real story is not about the differences between chimpanzees and humans, but instead the differences from one human to another. We know of no data with which to tally the exhaustive list of species found in an individual chimpanzee, or, for that matter, any individual human, but our general understanding



**Figure 1. The Known Number of Species of Parasites and Pathogens That Regularly Inhabit Chimpanzees and Humans, Respectively.** Whereas only about 40 species are estimated to inhabit chimpanzees [5] (left bar), more than 2000 [6,7] may parasitize humans (middle bar, unbroken line). Our expert opinion is that the true number of parasites of humans is at least 1000 more (middle bar, broken line) and perhaps even 2000 more. Very few of these species are found in both host species. The bar on the right-hand side shows the maximum number of human parasites and pathogens that are well studied ( $n = 10$ ), where to be well studied a species must be well understood with regard to its natural history, but also have had its distribution mapped well at a global scale; estimate from [11]. The three bars would all be dwarfed by the magnitude of the total number of associates (parasites, pathogens, and mutualists) of humans (and of our associates (not shown)). The parasites, pathogens and mutualists of are associates influence us too, yet many do not even yet have names. These associates of our associates almost certainly include, collectively, several hundred thousand species.

goes like this. The average individual chimpanzee hosts a relatively large proportion of all of those pathogens and parasites known from all chimpanzees. Let us posit 10%. Hunter-gatherer humans are likely to have hosted something similar, including many worms and protists. Agricultural humans in traditional rural societies likely have tens of kinds of parasites and pathogens – a couple of worms, many protists, malaria parasites, and more. But the most remarkable part of this story is what is going on in developed countries. With improved sanitation and public health,

the average person in those countries has very few parasites and pathogens, and those they do have are dominated by relatively innocuous viruses such as those that cause the common cold [8]. Despite there being more than two thousand parasite and pathogen species that can infect humans, most humans in developed countries are infected by very few. We sit beneath an enormous wave that is held back by vaccinations, sanitation, hand washing, and other aspects of development we take for granted, and ultimately driven by another unique feature of humans: our ability to accumulate knowledge and pass it to others.

Recently, Martin Blaser (among others) has argued that one of the biggest changes we face today is due to changes in the species of beneficial bacteria in our guts due to, among other things, the overuse of antibiotics. Here, the focus drifts from parasites and pathogens to other symbionts, namely the commensal and mutualistic bacteria. We have also shown that human skin microbes are different from those of other primates [9]. *Staphylococcus* bacteria, in particular, appear more common in humans than in chimpanzees or gorillas. This shift is, at least in part, due to our modern hygiene and product use [10].

Ultimately, it is only in light of a perspective that is both evolutionary and sufficiently holistic to include commensal bacteria, parasites, and pathogens, that our newer modern problems – chronic inflammatory diseases such as Crohn's disease, heart disease, and even our allergies – fully make sense. We have not just changed our gut microbes. We have changed our web of interactions. We are collectively connected to more species than ever before. Yet, individually we are connected to far fewer of these species. It will take decades to fully understand the consequences of this shift for how our bodies work, decades to make sense of who, relative to chimpanzees and the rest of life, we really are. What is certain is that

in terms of the synanthrome – a term we coin here in reference to the beneficial, costly, or neutral species with which we interact or have interacted – we are potentially unlike any other species on Earth that has ever lived.

Now is a time to reflect upon which interactions with other species we should have. There is, of course, no perfect synanthrome. The species that offer the greatest benefits will always depend on our lifestyle, genes, and culture, on who we are and what we desire. A species that provides a benefit in one context may prove detrimental in another (as is the case with some worms). But in order to know which interactions we really want, whether in confining ourselves to parasites, pathogens, and bacterial mutualists, or expanding to also consider crops and domesticated animals, requires us to know those species. In the past, scholars called for the intensive study of all the species in a park in Costa Rica (Guanacaste) or a less diverse park in the southeastern US (the Great Smoky Mountains National Park). Separately, studies on humans have sought to inventory the sum total of the genes that make us human (the Human Genome Project) or the totality of the microbes (typically bacteria) in and on healthy humans (the Human Microbiome Project).

We call for an effort that builds upon these efforts to inventory life, a Global Synanthrome Project. The project would be a full survey of the species with which humans interact around the world – be they parasites, pathogens, commensal bacteria, or crops – and how those are changing. To be successful, such a study needs to include both sequencing-based approaches and natural history and organismal biology (focusing on the gut, for example, it would need to include both bioinformaticians and parasitologists). Such a survey might require us to study, in detail, hundreds of thousands of species. It would also require us to study the species our associates depend upon, be they the gut microbes

of face mites or the pollinators of cacao trees. Yet this is the real task before us if we are to understand ourselves, understand how we have changed, and how we might hope to change in the future. We have the approaches necessary to achieve such an effort. Sequencing approaches are increasingly cheap, ecological and evolutionary theories are as rich and useful as they have ever been, and traditional natural historians are still around (though not for very long in some fields). Now is the time for the detailed understanding of the natural history of each of the tens of thousands of species with which each of us interacts or fails to interact, the species that, in all of the geographic and social complexity, make

us human far more than do the modest changes in our own genes.

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