Research project – 2024/2025

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Paleogenomic insights into dispersal patterns and selection processes in the history of cat domestication

1. State of the art

Genetic evidence from modern wild and domestic cats demonstrated that the ancestor of domestic cats is the Near Eastern and North African wildcat, *Felis silvestris lybica*[1]. While the first archaeological evidence of cat-human association comes from Cyprus and the Levant[2], the analysis of genome-wide data from >70 archaeological cat remains in Europe points to an origin of domestic cats in North Africa, most likely in Egypt, from where they dispersed probably 2500 years ago[3].

After their dispersal, domestic cats have been linked to humans for centuries until present-day and yet, the selection and development of the different fancy breeds occurred recently, during the 19th century AD[4]. However, selection of peculiar aesthetic traits may have occurred in the last millennium. For example, in 2017 *Ottoni et al.*[5] were able to date the emergence of the blotched coat pattern in domestic cats to the Middle Ages. All in all, the domestic cat's appearance is very close to its wild relative, hinting at behaviour as a first target of selection at the onset of its domestication[6].

2. Research objectives

2a. Refining the introduction of the domestic cat in Europe

The first remains identified as domestic cats in Europe are dated to the Roman age, and their dispersal north of the Alps is traditionally associated with the Roman army. However, archaeozoological data remain contentious and a possible introduction of cats to Europe during the Iron Age cannot be ruled out. Furthermore, ancient DNA (aDNA) data suggest possible pre-Roman introduction of cats with the Punics in the Mediterranean, probably from a source population in Northwest Africa[3].

The first objective of this PhD project will be to refine the timescale of cat introduction to Europe by conducting paleogenomic analyses on novel archaeological samples (n=40) dated to the Iron Age from France, Italy and the Netherlands. Based on previous data about DNA preservation, I aim at generating genome-wide data from at least half of them, thus making it possible to test whether cats were introduced to Europe in pre-Roman times and filling a major gap of knowledge in the current literature.

2b. Investigating selection patterns across time

The second objective of this PhD project will focus on selection patterns through time. Three categories of traits will be investigated:

- Behavioural genes which were identified in 2014 by *Montague et al.*[6] related to fear conditioning (*PCDHA1* and *PCDHB4*), memory (*GRIA1* and *DCC*) or neurological conditions (*PLEKHH1*).

- SNPs which were identified for different aesthetic traits. For example hair length (*FGF5*[7]) or another physical trait, usually associated with domestication, white spotting (*KIT*[8]).
- SNPs associated with diseases, for example polycystic kidney disease (*PKD1*), the most common kidney disease in domestic cats[9].

These loci will be investigated on different types of cat and wildcat samples in order to compare their evolution in time. Most of the ancient samples selected were already processed, showing 30% of endogenous yields. A deeper sequencing of these samples will be done to retrieve a medium coverage of ~4X, which was previously demonstrated to be sufficient for the analysis of selection in ancient genomes[10,11,12]. High-coverage (~15X) modern samples sequenced for the FELIX project (PI Claudio Ottoni, supervisor of this PhD project) or retrieved from the literature will also be used without any need of a deeper sequencing. In total, five types of samples will be studied:

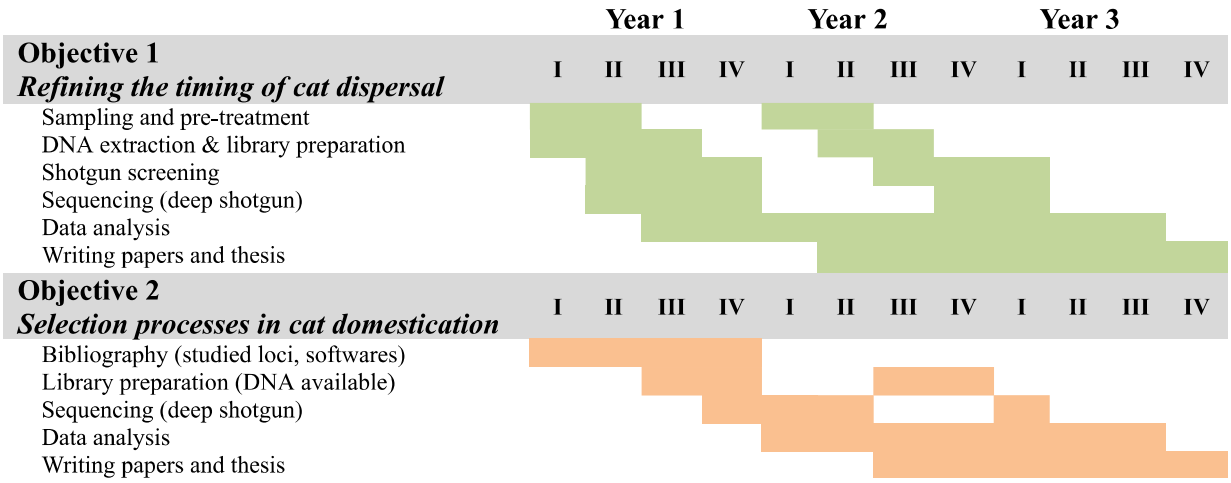
- European wildcats that pre-date the cat domestication (n=11). These samples are either dated to the Mesolithic or the Neolithic and weren't associated with humans, meaning that no artificial selection acted on them.
- Earliest samples of domestic cats found in Europe (n=7, at least). Samples without (or with minimal) gene flow from European wildcats will be selected to avoid any bias arising from this admixture.
- More recent domestic cat samples spanning from the Middle Ages to the 19th century AD, covering about 1,000 years (n=18). These samples will be used to determine the appearance of peculiar traits that arose recently.
- Samples of Middle Eastern and North African modern wildcats (n=18). These will represent a set of direct relatives to domestic cats which didn't go under any type of human selection.
- Finally, genomes of modern bred and random-bred domestic cats will be added to these studies (n=25). These genomes are already available at a high coverage from the literature, the project *99 lives*[13] already sequenced 35 breeds which can be used in this project, taking into account their geographical origin as well as the selective breeding they underwent.

3. Materials and Methods

For the first part of the project, the European samples, which are already available, will be processed and sequenced following the protocol of *Meyer & Kircher (2010)*[14] for the library preparation. Retrieving their mtDNA and nDNA will allow different analyses such as determining their mtDNA clade using BEAST2[15] but also conclude a species identification using a PCA, with the package smartsnps[16], and test other population genetic analyses such as a possible admixture with European wildcats using f4-ratios with ADMIXTOOLS[17].

As for the selection signals, in genes related to behaviour, for which mutations weren't identified, it is possible to compare different metrics. A selection signal can be detected by looking at the Linkage Disequilibrium (LD), the nucleotide diversity (π) or the Tajima test to compute the number of polymorphic sites (θ_n). For the other mutations, for which causal SNPs were found, a genotyping with the PALEOMIX pipeline as done by *Schubert et al., 2014*[18] or a genotype likelihood with the software ANGSD[19] as done in *Librado et al., 2017*[11] can be performed to check for their presence.

4. Gantt chart and work plan



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