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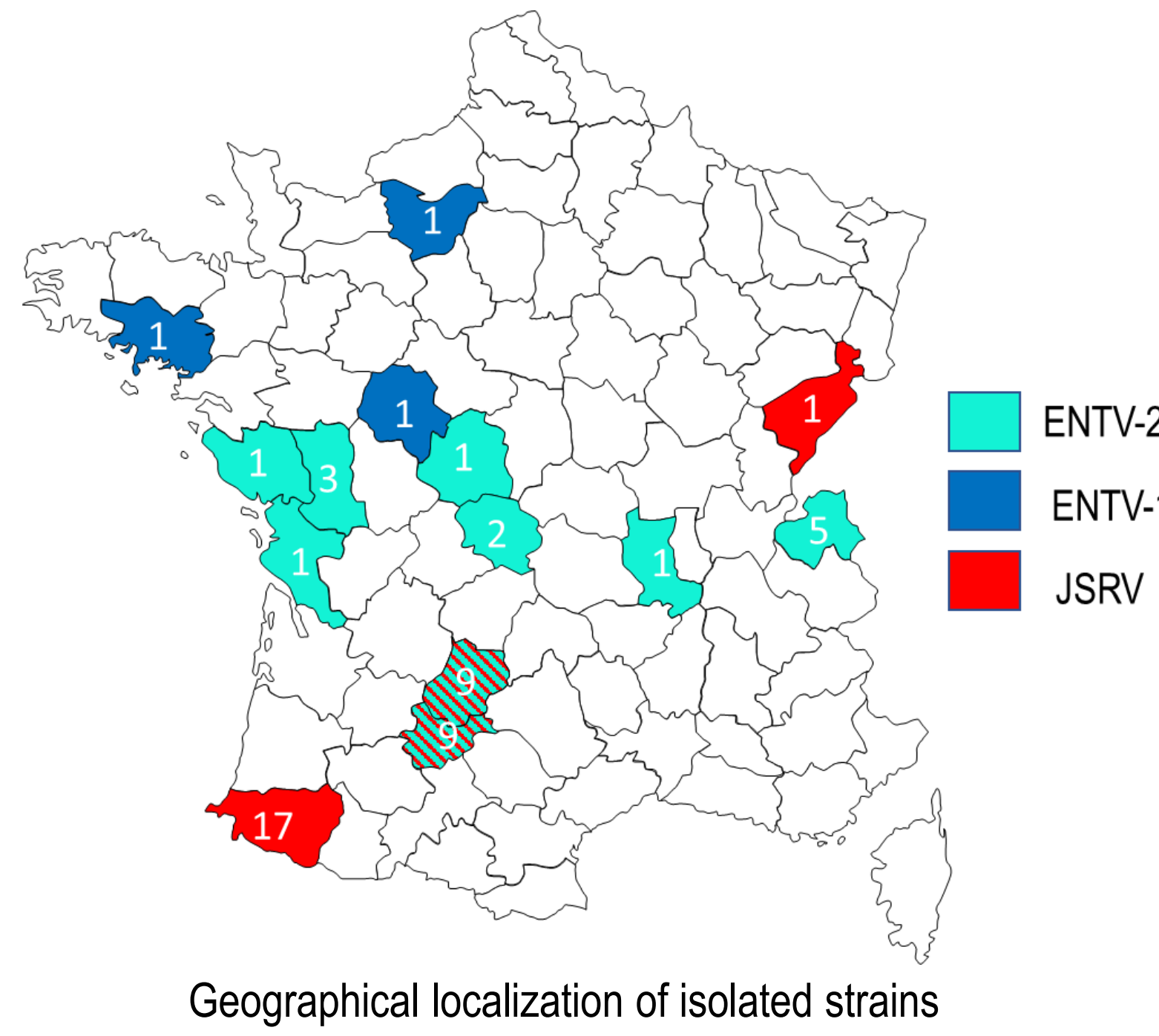
DIVERSITY OF β -RETROVIRUSES CAUSING RESPIRATORY CANCERS IN SMALL RUMINANTS

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CONTEXT AND OBJECTIVES

- ☑ **Oncogenic β -retroviruses** are responsible for respiratory cancers in small ruminants. While **JSRV** (Jaagsiekte Sheep RetroVirus) induces **lung cancers** in sheep, **ENTV** (Enzootic Nasal Tumor Virus) induces **nasal tumors** in sheep for (ENTV-1) and goats for (ENTV-2). The **envelop** (Env) **glycoprotein**, especially the intracytoplasmic tail of the transmembrane region, carries the transforming capacity and is referred as the **main oncogenic determinant**
- ☑ Multiples copies of highly related **β -endogenous retroviruses** (β -ERVs) resulting from ancestral infections of germinal cells during evolution are **present in the small ruminant genomes**
- ☑ JSRV and ENTV are endemic in many countries. As we observe in France, the **clinical expression varies** in terms of severity and morbidity/mortality rates in flocks, from isolated/ **sporadic** cases to **cancer outbreaks**



OBJECTIVES

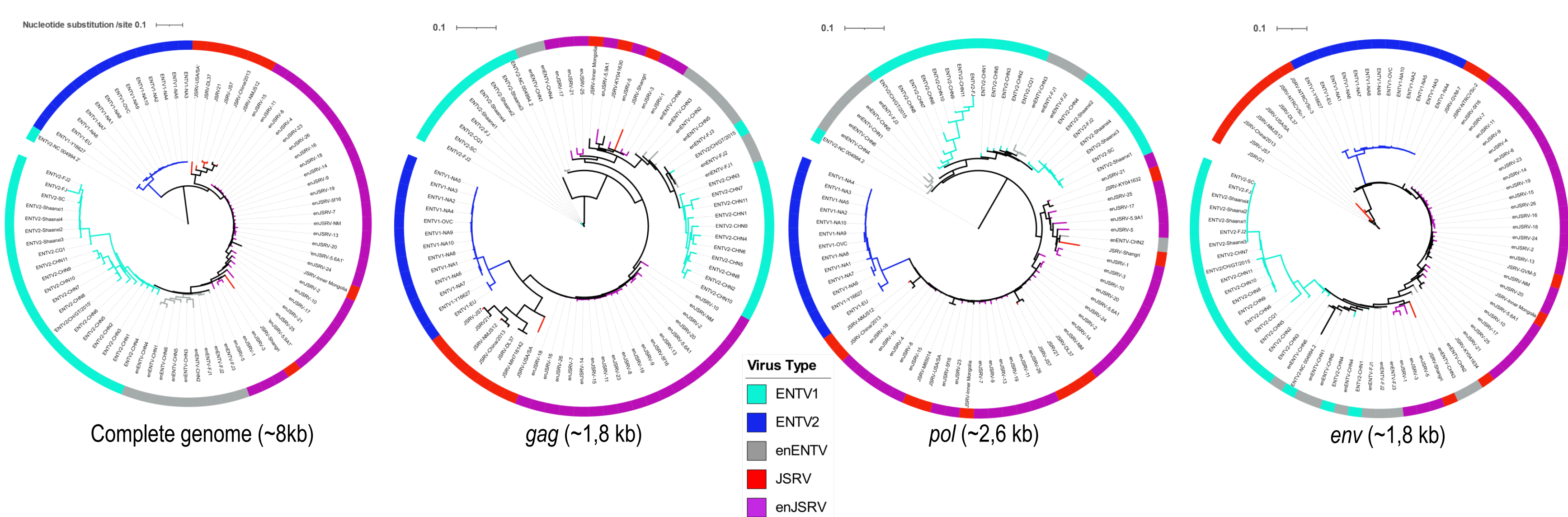
What is the diversity of retroviruses circulating in France and how does their diversity relate to the clinical expression?

We focused on the genetic characterization of the oncogenic β retroviruses (30 JSRV, 3 ENTV-1 and 21 ENTV-2) from various regions of France (31 flocks), and on their sequence analysis to identify specific strains associated with increased clinical expression in some flocks.

METHODS AND RESULTS

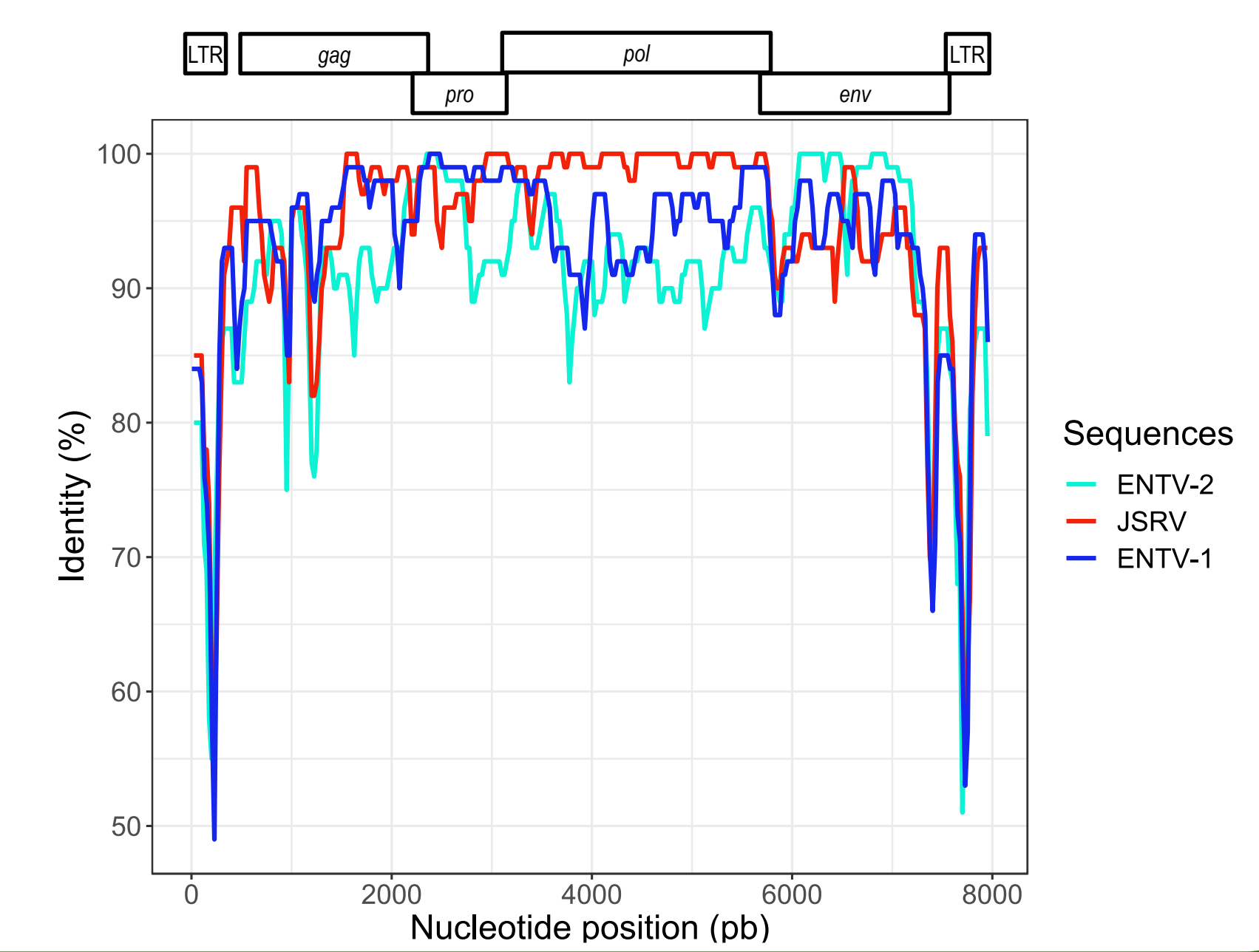
1 EXOGENOUS β -RETROVIRUS ARE CLOSELY RELATED THEIR ENDOGENOUS COUNTERPARTS

Phylogenetic reconstruction based on JSRV, ENTV-1, ENTV-2 and small ruminant ERV (published in public databases)



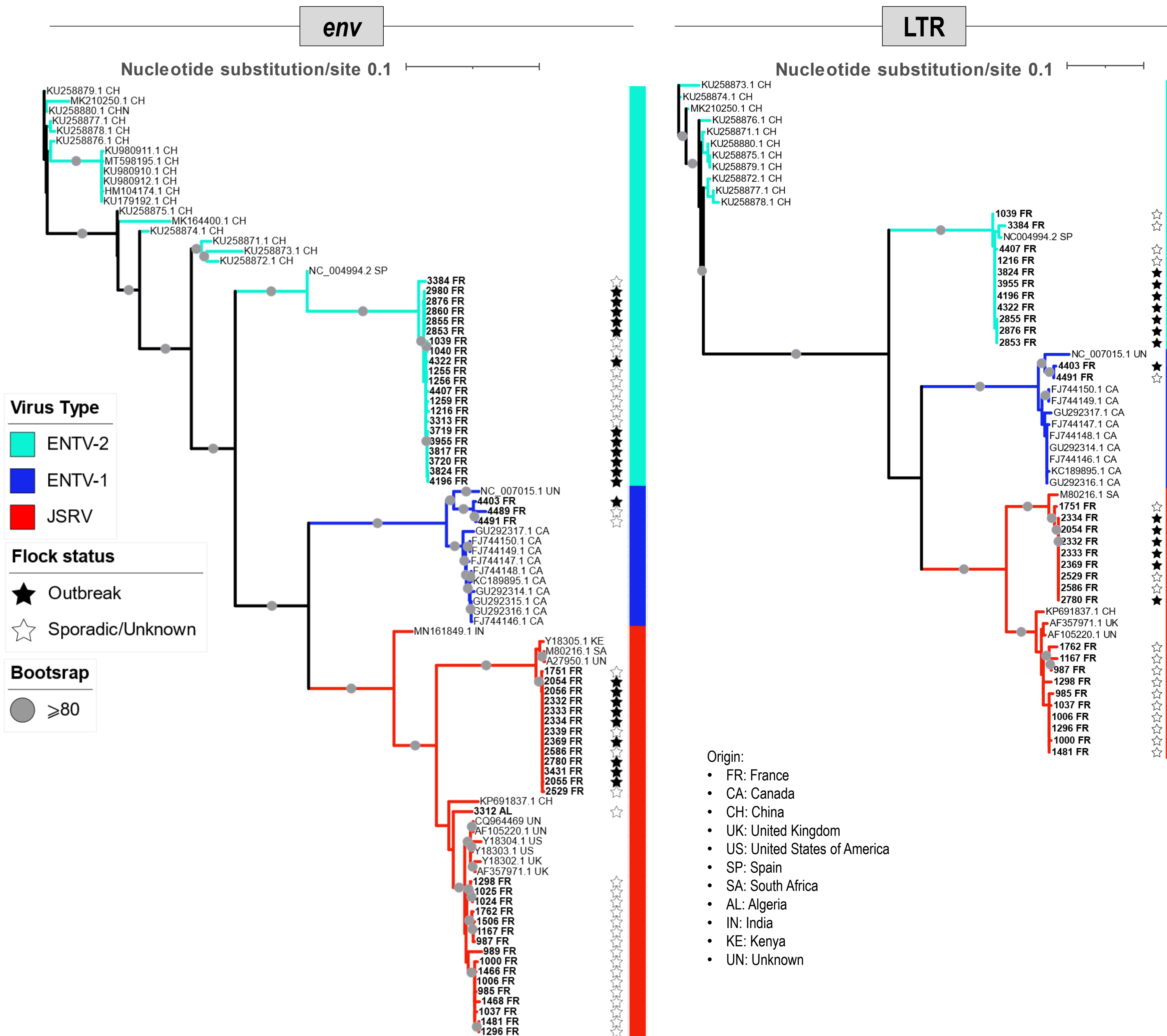
- ☑ Compared to ERVs, only short and localized regions are **specific of the exogenous β -retroviruses** located in the terminal part of *env* and the U3 region of both LTRs
- ☑ We have developed a **highly specific strategy** to selectively amplified the **exogenous ENTV** and JSRV genomes

Identity plot (nt) along the β -retrovirus genome against a consensus sequence of related ERVs



2 DIVERSITY OF β -RETROVIRUSES CIRCULATING IN FRANCE

Phylogenetic reconstructions based on French JSRVs and ENTVs in the *env* coding and LTR non-coding regions (ML Tree with a 500 bootstrap replicates; strains sequenced in this project are indicated in bold characters)

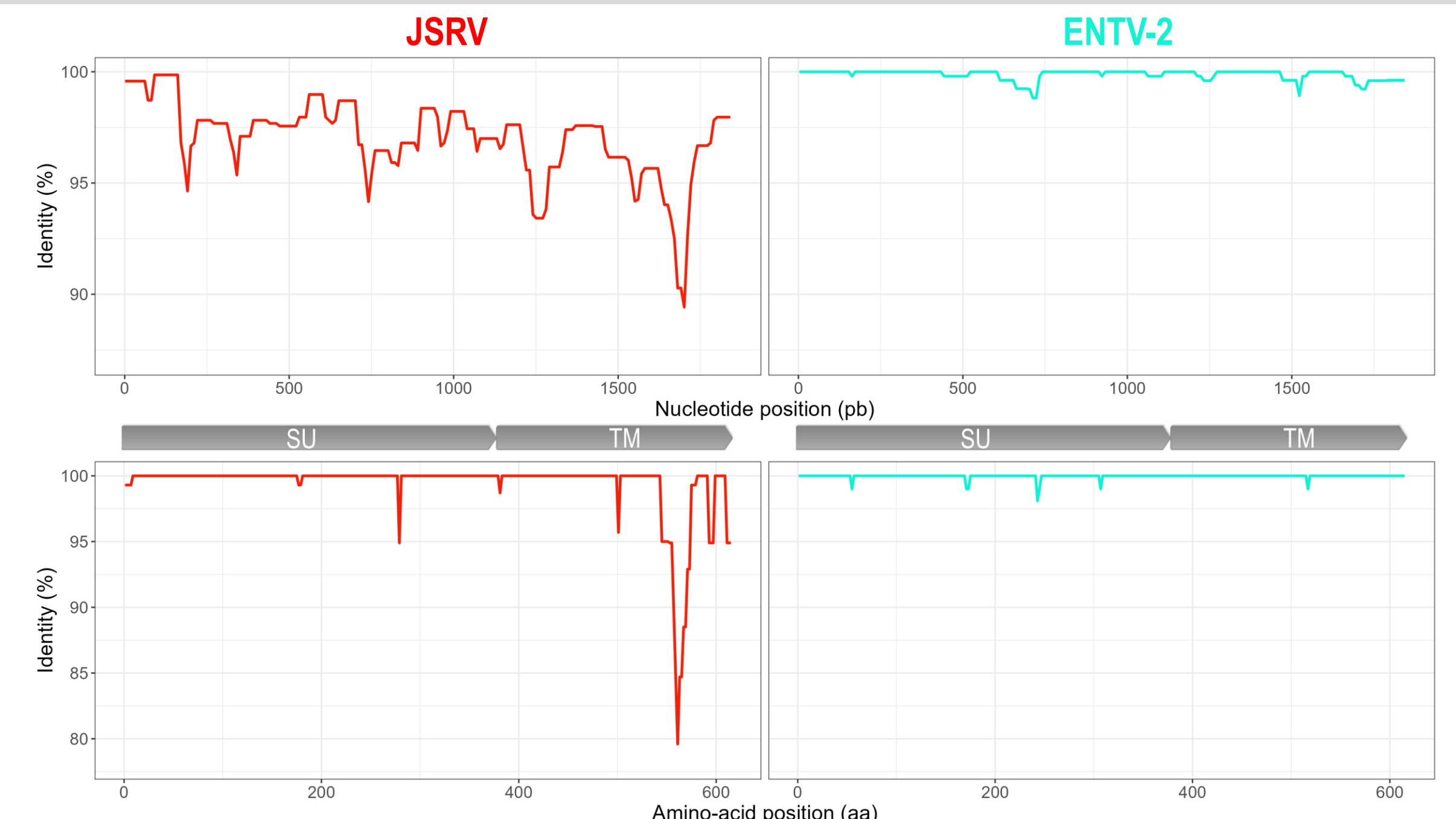


Based on their sequences in the LTR and *env* regions, we report on :

- ☑ the **first genetic characterization** of JSRV, ENTV-1 and ENTV-2 strains circulating in France
- ☑ the relative **stability** of JSRVs and ENTVs, sampled from geographically distinct French areas with ~95% of nt similarity
- ☑ the **stability of the circulating strain** for a given ovine or caprine flock with over 98% similarity in nt sequences
- ☑ the circulation of **two genetically distinct groups of JSRV**, one being often associated to **more severe clinical expression** (in terms of morbidity/ mortality rates)

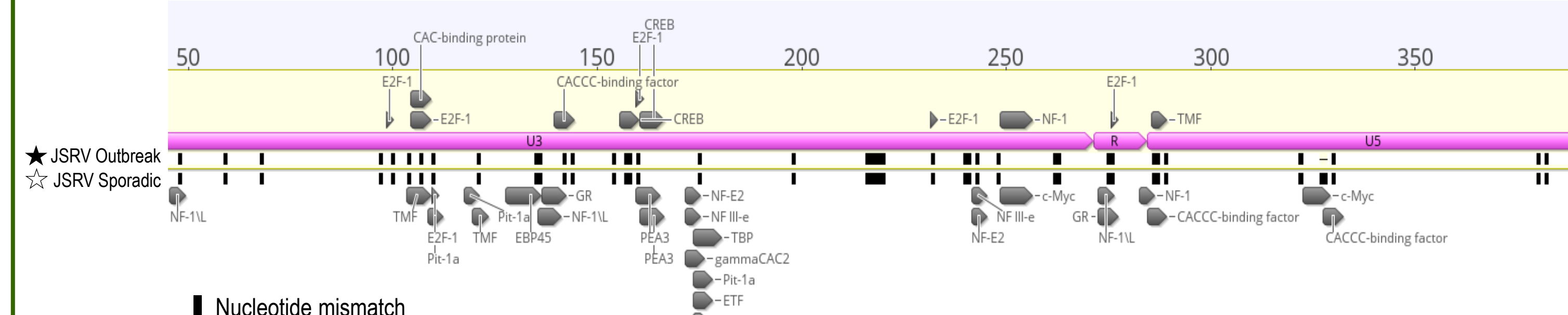
3 IDENTIFICATION OF GENETIC SIGNATURES POTENTIALLY ASSOCIATED WITH DISEASE EXPRESSION IN FLOCKS

Identity (nt and aa) along the *env* gene coding for the Surface (SU) and Transmembrane (TM) glycoprotein



- ☑ In *env*, most variations between JSRV strains are located in the intracytoplasmic tail of the 3' part of the **transmembrane domain (TM)**, implicated in the transformation process

Differences in transcription factor binding-sites can be identified in JSRV LTRs, accordingly to the severity of the disease expression in a given flock (predicted by *tfscan*)



- ☑ Identification of **distinct transcription factor binding-sites** between strains isolated from **outbreaks and sporadic events**

CONCLUSIONS/ PERSPECTIVES

- ☑ **First report** on French strains of oncogenic β -retroviruses responsible for cancers in sheep and goats
- ☑ In France, **low sequence diversity of ENTV** while **JSRV strains are more diverse**
- ☑ Association of **JSRV-genetic signatures with the severity of disease**
- ☑ Perspectives : Test of the impact of the genetic signatures on the **oncogenic properties of JSRV**