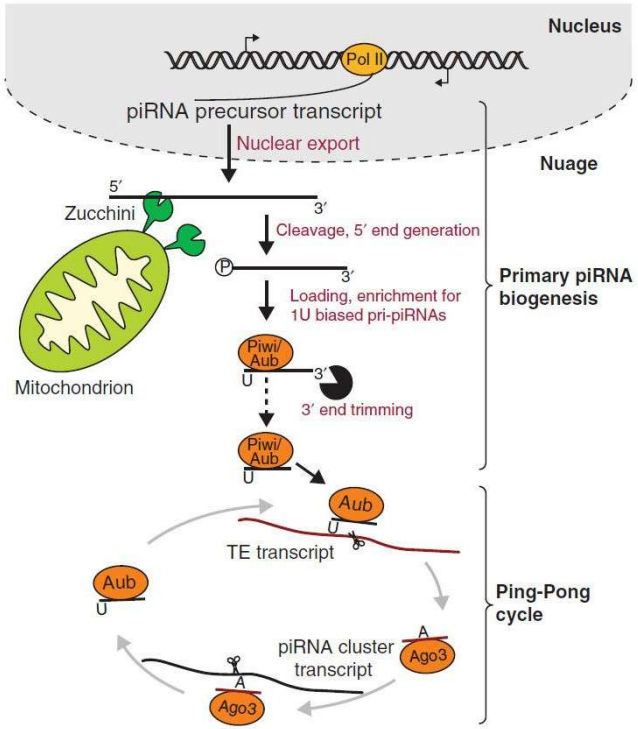
Oupsi? :D

Let’s do this boiiiis

Introduction

piRNA : PIWI-interacting RNA (PIWI : protein)

In germline cells : the main function results in the formation of a piRNA-PIWI silencing complex which inhibits the expression of transposons.
In somatic cells : unknown role.



Introduction

Decreasing of piRNAs in cells derived from pluripotent cells' from Parkinson's disease patients.

Experience on animals having SLA or tauopathies : many increased and decreased transposable elements →piRNAs could be potential biomarkers for neurodegenerative disease.

Goal of the study : identify the impact of piRNAs in Parkinson's disease

length features. Somatic piRNAs show shorter and more evenly distributed lengths than germline piRNAs (Figure 6). According to the ping-pong cycle biogenesis pathway, tissues

genes in germline cells [17]. To our surprise, both brain tissue and testis tissue
richment results for "Parkinson's disease" and "Pathways of Neurodegenerati
diseases", respectively (Figure 5). However, the function of these sense-piRNAs

Intro: Problématique, objectif de l'étude, contexte médical

rôles non-connus etc…

Steven my boi, you're doing this shit

To determine the significance of somatic piRNAs in human disease, we detected 296 piRNAs in the prefrontal cortex of which 20 piRNA expression levels were significantly different in PD; and 508 piRNAs in amygdala of which 55 piRNA expression levels were significantly different in PD (Figure 7a). Among these, one piRNA (piR-hsa-748391) was expressed differently in PD in both prefrontal cortex and amygdala tissues. Unfortunately, none of 3′UTR derived piRNAs from neurodegeneration-related genes mentioned above

What is known : piRNAs in germline (cf intro known roles) ?

piRNAs are found in somatic cells but role is unclear

In PD, it seems that piRNAs expression is different in brain tissues prefrontal cortex and amygdala

Role in PD and Neurodegenerative pathways ? Function is indistinct.

Authors wanted to know role of piRNAs in PD

example, L1 can induce mosaicism in the neural genome [32]; and Alu is hypothesi
to be related to human intelligence, cognition, and neurodegeneration [33]. Theref

complementary [22,23]. In contrast, the piRNA biogenesis pathway in somatic cells sho
a distinct process [24–26]; however, the details remain elusive and controversial, especia
in mammals. Many studies suggests somatic piRNAs exist and function in body regen
ation [26,27], cancer [28], embryonic development [29], and neural development [30].

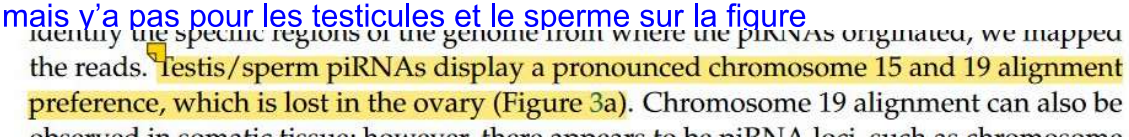
comparison piRNA expression between somatic and germline tissues

ularly through microglia [59,60]. A previous study indicated piRNAs were
in neuronal cells derived from induced pluripotent stem cells of sporadic PD
pared to controls [61]. In the study, SINE and LINE-derived piRNAs were
d. In addition, two studies found different expression patterns of piRNAs in

transposable elements in human AD tissues [63]. These results suggest that piRNA
be potential biomarkers for age-related neurodegenerative disease, including PD. No
less, existing knowledge concerning piRNAs in PD remains obscure. Therefore, d

Methods/Summary

Une personne suffit pour la méthodo, deux personnes pour résultats? OK
Steven tu avais détecté une connerie dans la méthodologie non?
Ils disent ça mais y'a pas pour les testicules et le sperme sur la figure


identify the specific regions of the genome from where the piRNAs originated, we mapped the reads. Testis/sperm piRNAs display a pronounced chromosome 15 and 19 alignment preference, which is lost in the ovary (Figure 3a). Chromosome 19 alignment can also be

So how did they do to study the implication of piRNAs in somatic cells and in PD ?

1. Pre-processing steps (Quality Control, adapter trimming length trimmering on small RNA datasets from GEO database) and piRNA annotation (mapping and annotation based on piRBase) - germline versus somatic cells

   Fig. 2

2. piRNA features investigation (chromosome distribution, genomic context, length distribution, ping-pong cycle) - germline versus somatic cells

   Fig. 3, 4, 5, 6

3. Comparative study between PD and control (differential expression analysis, gene enrichment analysis

   Fig. 7, 8, 9, 10, 11

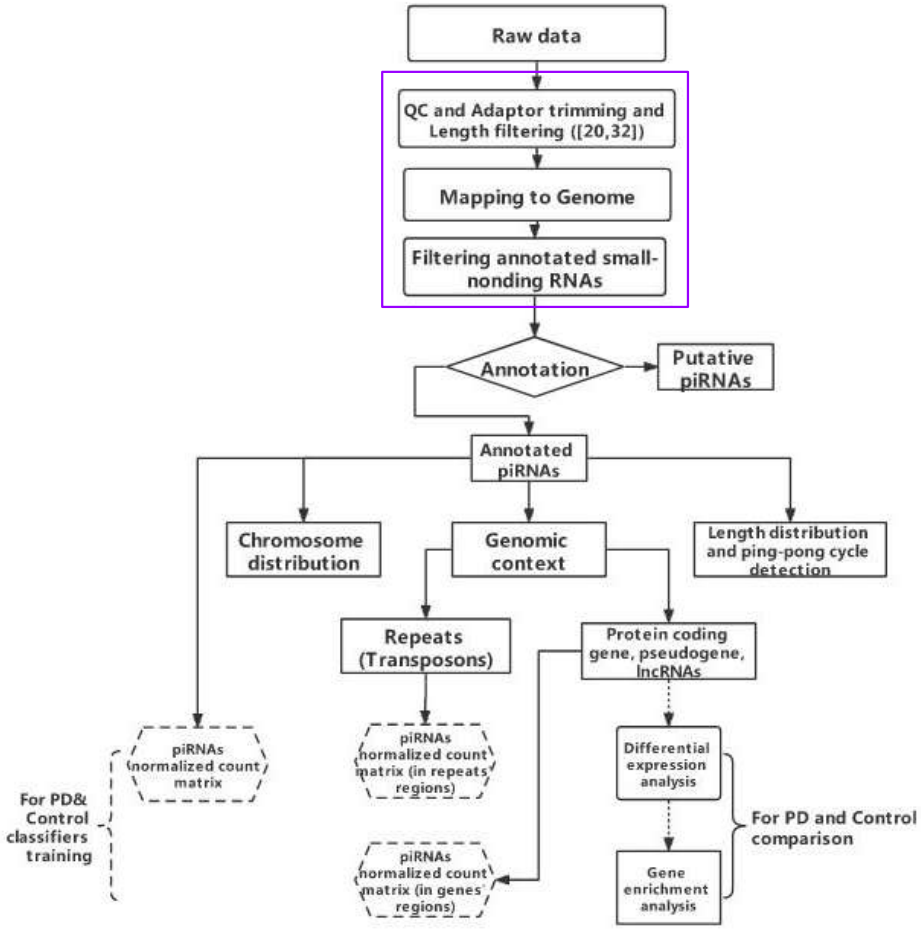


Figure 1. Workflow of this study. The raw data length filtered (20,32) is shown in brackets.

Methods - Pre-processing

WorkFlow (2.1)

ça pourrait être intéressant de

détailler la partie surlignée?

2.3. *Pre-Processing and piRNAs Annotation*

Sequenced raw data were adaptor trimmed and size filtered (20–32 nucleotides) by cutadapt (v2.8) [82]. We then aligned the processed sequencing data to hg38 Human Genome assembly [83] by bowtie (v1.2.3) [84] with one mismatch tolerance, and alignments with more than 50 distinct positions restrained. To filter other small non-coding RNAs (rRNAs, tRNAs, miRNAs, scaRNAs, snoRNAs, miscRNAs, scRNAs, sRNAs, and snRNA) in our datasets, we created an aggregated small non-coding RNA annotation file based upon UCSC [85], RefSeq [86], Gencode [87], DASHR [88], and Ensemble databases and annotations [83]. We excluded reads aligned to these other small non-coding RNAs from further investigation. We used featureCounts (v2.0.0) [89] and piRNA annotation file download from piRbase [90] to annotate piRNAs in the remainder of the reads. The reads annotated by piRBase were considered as annotated piRNAs in our study. The general workflow of the study is shown below as Figure 1.

Table 1. Description of small RNA datasets curated for the analysis.

Tissue	Accession	Sample Size	Library Size
Testis	PRJNA196749	3	6.84–25.30 million
Sperm	PRJNA564759	102	0.36–1.63 million
Ovary	PRJNA272542	12 Note: 4 adult ovaries; 4 ovaries from 1st trimester embryos; 4 ovaries from 2st trimester embryos	13.3–15.8 million
Dorsolateral Prefrontal Cortex (DLPFC)	PRJNA185476	4	6–12.25 million
Pancreas	PRJNA490335	3	12.2–12.5 million
Knee synovial tissues	PRJNA389258	10	8.39–17.21 million
Liver	PRJNA246372	4	5.83–40.70 million

Table 1. *Cont.*

Tissue	Accession	Sample Size	Library Size
Prefrontal cortex (PFC)	PRJNA295431 PRJNA272617	26 (Parkinson's disease) Note: including 17 Parkinson's disease (PD); 9 Parkinson's disease with dementia (PDD) 25 (Control)	6.09–33.40 million
Amygdala	PRJNA381204	14 (Parkinson's disease) Note: including 7 premotor stage; 7 motor stage 14 (Control)	13.5–17.7 million
Blood (extracellular vesicles)	PRJNA655240	9 (Parkinson's disease) Note: in each sample, both large (LEV) and small extracelluar vesciles (SEVs) were tested 6 (Control) Note: in each sample, both large (LEV) and small extracelluar vesciles (SEVs) were tested	2.37–30.7 million

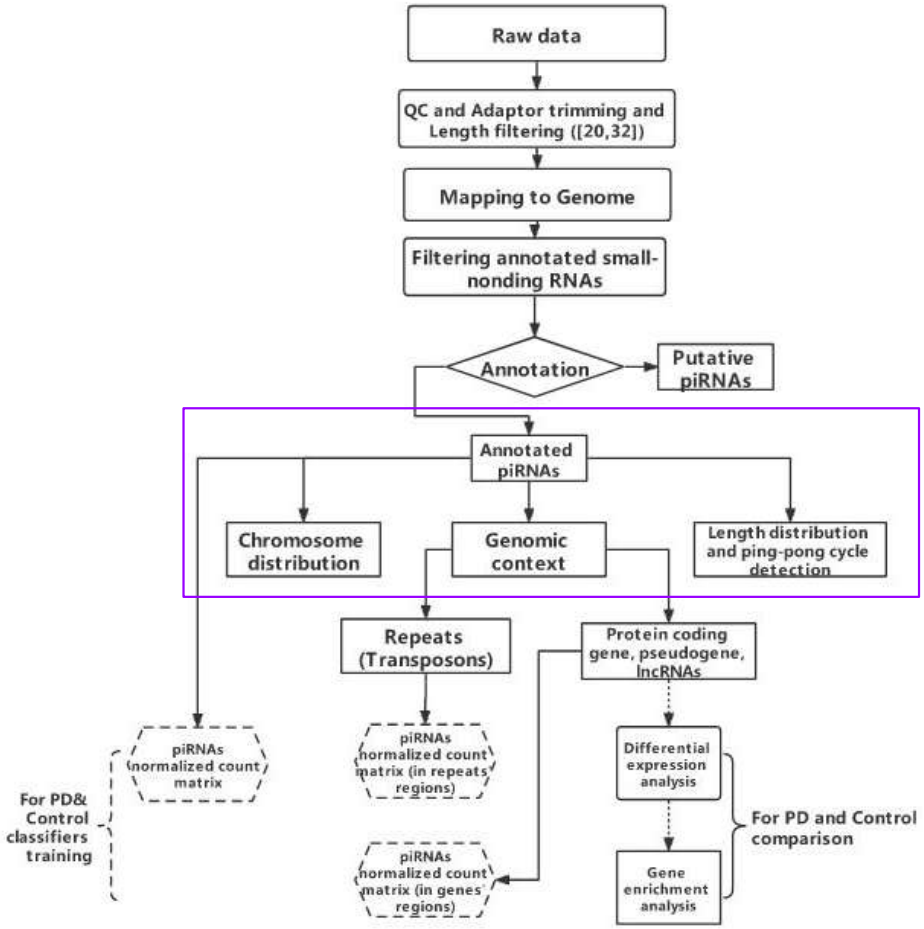


Figure 1. Workflow of this study. The raw data length filtered (20,32) is shown in brackets.

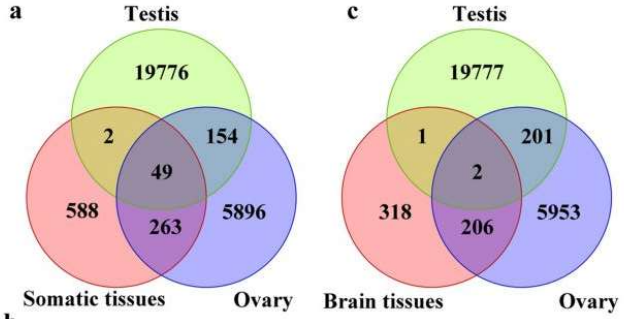
Methods

results:

3.1. piRNA Expression in Somatic Cells and Comparison to Germline Cell

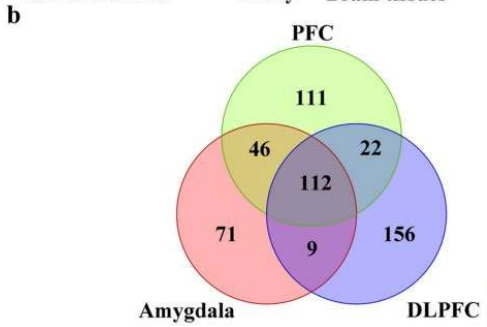
extracting and identifying piRNAs from next generation sequencing (NGS) datasets. The pipeline is shown in (Figure 1). As the ovarian tissue dataset has a different experimental design and sequencing depth with others, piRNAs were considered expressed if reads were >2 in all samples or reads > 5 in 50% of samples, while for other tissues, the standard was reads > 2 in all samples or reads > 10 in 50%. We first compared piRNAs from somatic tissue to the testis and ovaries. The total number of piRNAs identified from the testis, ovary, and somatic tissue were 19981, 6363, and 902, respectively (Figure 2a). Consistent with previous studies, we identified a large number of testis piRNAs and a small number of somatic RNAs [102]. There were 49 common piRNAs between tissues studied, 51 between

previous studies, we identified a large number of testis piRNAs and a small number of somatic RNAs [102]. There were 49 common piRNAs between tissues studied, 51 between somatic and testis tissues, and 312 between somatic and ovaries, representing >30% of all somatic piRNAs. When the brain piRNAs were considered, the total number of piRNAs were 527 (Figure 2b). There was a dramatic reduction in piRNAs overlapping with testis, 3



Beaucoup moins de partage de PiRNA entre testis/brain que ovaire/brain /!\ => warning, somatic c'est pas glorieux non plus, ça se superpose +/-

in total, while 208 overlapped with ovaries. When we further compared brain regions, we observed that piRNAs were widely dispersed between the amygdala, prefrontal cortex, and dorsal lateral prefrontal cortex (Figure 2c). The expression pattern of somatic piRNA types

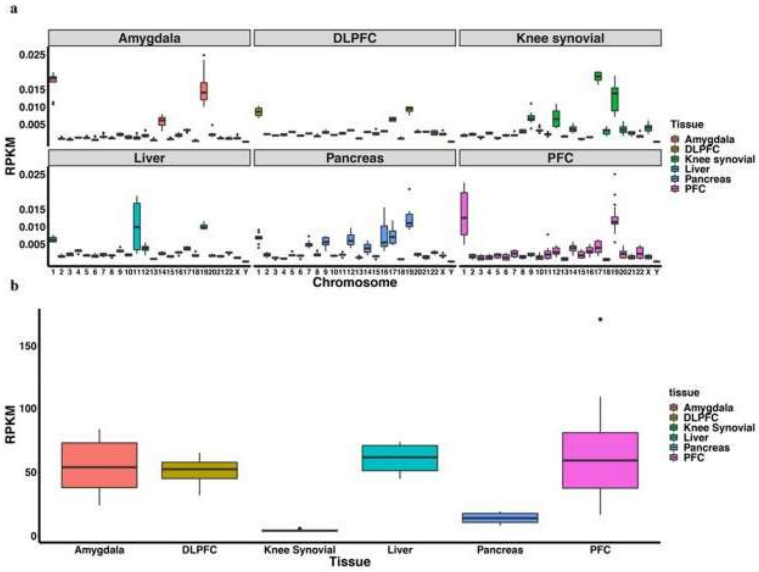


dorsal lateral prefrontal cortex (Figure 2c). The expression pattern of somatic piRNA types appears to be tissue-specific with a large proportion of different piRNAs in the germline (testis, sperm, and ovary) (Figure 2a–c) (Supplementary Figure S1), which suggests that somatic piRNAs might function differently than those from germline piRNAs.

Figure 2. Venn plots of piRNAs identified from germline and somatic tissues. The number of piRNA types among somatic (dorsolateral prefrontal cortex, prefrontal cortex, amygdala, pancreas, liver, and knee synovial), germline tissues (testis, sperm, and ovary), and brain tissues (dorsolateral prefrontal cortex (DLPFC), prefrontal cortex (PFC), and amygdala) were compared. (**a**) Comparison between somatic and germline tissues. (**b**) Comparison between brain and germline tissues. (**c**) Comparison between different brain regions.

Conclusion sur le fonctionnement un peu rapide pour moi. tissu germinal immensément différent en comparaison par rapport au somatique.

ok, piRNA viennent d'un loci spécifique, ici ils identifient de quel chromosome viennent chaque piRNA pour chaque tissu



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identify the specific regions of the genome from where the piRNAs originated, we mapped the reads. Testis/sperm piRNAs display a pronounced chromosome 15 and 19 alignment preference, which is lost in the ovary (Figure 3a). Chromosome 19 alignment can also be observed in somatic tissue; however, there appears to be piRNA loci, such as chromosome

pas de trace sur schéma, on en parle mais on précise la connerie

the reads. Testis/sperm piRNAs display a pronounced chromosome 15 and 19 alignment preference, which is lost in the ovary (Figure 3a). Chromosome 19 alignment can also be observed in somatic tissue; however, there appears to be piRNA loci, such as chromosome 4 for ovary, 1 for brain tissues, liver, and pancreas, and 11 for liver (Figure 3a). Somatic piRNAs also show a high mitochondrial chromosome alignment rate among all three brain

observed in somatic tissue; however, there appears to be piRNA loci, such as chromosome 4 for ovary, 1 for brain tissues, liver, and pancreas, and 11 for liver (Figure 3a). Somatic piRNAs also show a high mitochondrial chromosome alignment rate among all three brain tissues studied and the liver in contrast to germline tissues (Figure 3b).

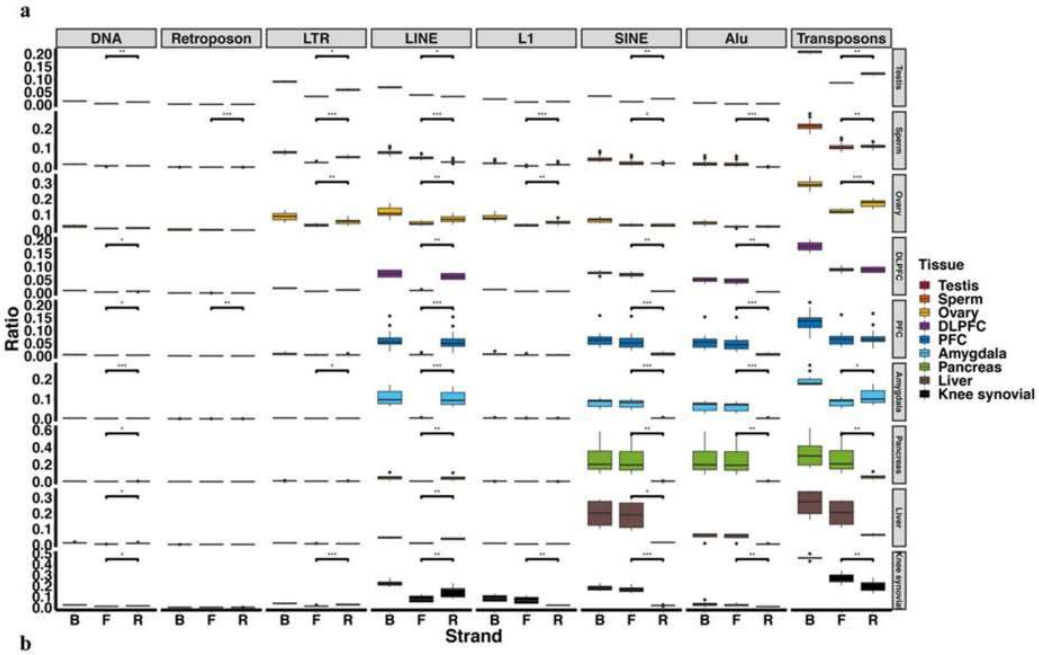
piRNA fonctionnent avec transposons normalement? on voulu vérifier si ça se passait pas correctement dans l'un des deux, PAF ça ne semble pas fonctionner normalement dans les deux en même temps => RIP

To determine whether somatic piRNAs were functioning via the well-established transposon suppressing pathway, we identified the transposon sequences aligned to the piRNAs. We unexpectedly detected a lower percentage (~20%) of piRNAs aligned to

transposon suppressing pathway, we identified the transposon sequences aligned to the piRNAs. We unexpectedly detected a lower percentage (~20%) of piRNAs aligned to transposon sequences in both somatic tissues and germline tissues (Figure 4a). This lower percentage in germline was also found by other studies [103,104]. Unlike other tissues, amygdala and germline piRNAs contain more reverse-stranded repeat transposons stranded. Considering the prevalent model related to piRNA-guided transposon silen

where the PIWI-piRNA complex interacts with a nascent transposon transcript, a higher reverse-stranded piRNA percentage might indicate that repressing transposon expression is a vital function in both amygdala and germline tissues. In LINE-alignment piRNAs, somatic

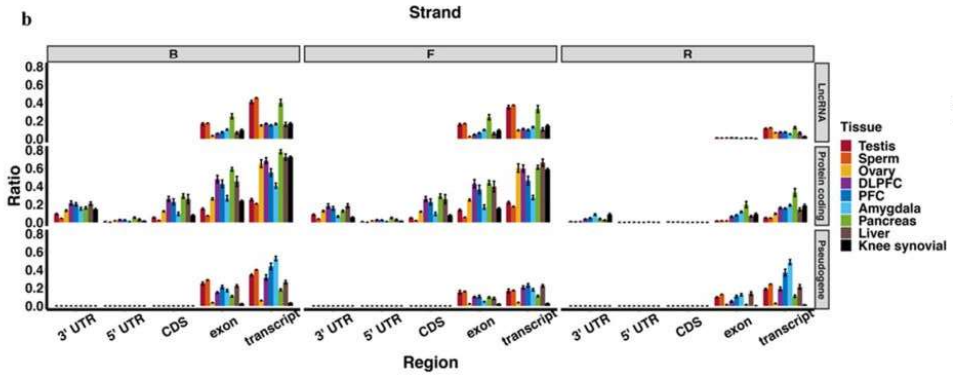
reverse-stranded piRNA percentage might indicate that repressing transposon expression is a vital function in both amygdala and germline tissues. In LINE-alignment piRNAs, somatic and ovarian piRNAs show a reverse-stranded preference, while testis and sperm piRNAs present the opposite. However, testis piRNAs show a reverse-stranded preference in SINE-alignment piRNAs, while somatic piRNAs are just the opposite (Figure 4a). Because LINE and SINE might have different impacts in somatic and germline tissues, their aligned-piRNAs might have varying regulatory functions.



LINE/SINE = rétro transposons! Je percute pas comment ils différencient preferebce reverse stranded

B=both? R = reverse F= forward

toujours même péché: déduction à partir de l'origine/quantité des piRNA de leur fonction, un peu foireux comme déduction?

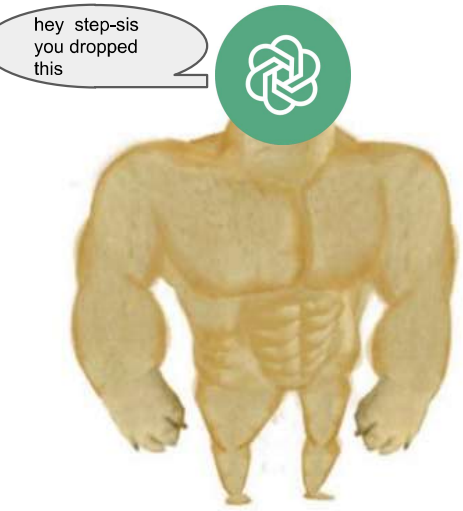


We also identified many piRNAs aligned to pseudogenes, which is more evident in testis and sperm tissue as their lower protein-coding gene alignment rate (Figure 4b).

A recent study suggested that some pseudogene-derived piRNAs have the potential to target and regulate their cognate protein-coding genes [106]. A more detailed study might

We observed that testis and sperm piRNAs showed a higher percentage of lncRNA-alignment (Figure 4b). These are mainly mammalian pachytene piRNAs, which are primarily generated from transposon-depleted lncRNAs and thought to regulate genes required for male fertility [17]. We detected a higher ratio of protein-coding derived piRNAs, especially in somatic tissues, suggesting a function different that in germline cells. This phenomenon is partly contributed by some coding-gene (~25%) containing transposon sequences in the 3′UTR [105]. Some studies demonstrated that these genes have the potential to be controlled by PIWI and transposon-derived piRNA complex [106], but it is more likely that there are more protein-coding-derived piRNAs that exist across tissues.

Currently the detailed function of coding-protein-derived piRNAs remains unknown.



L'enrichissement KEGG (Kyoto Encyclopedia of Genes and Genomes) est une méthode d'analyse bioinformatique utilisée pour interpréter des ensembles de gènes ou de protéines en fonction de leur pertinence dans des voies biologiques spécifiques. KEGG est une base de données qui catalogue les informations sur les voies métaboliques, les fonctions cellulaires, les maladies et d'autres aspects liés aux gènes et aux protéines.

Le processus d'enrichissement KEGG implique généralement les étapes suivantes :

1. **Identification des gènes d'intérêt :** Vous avez un ensemble de gènes ou de protéines que vous souhaitez analyser, par exemple, ceux qui sont différentiellement exprimés dans une expérience particulière.
2. **Comparaison avec la base de données KEGG :** Les gènes ou protéines d'intérêt sont comparés à la base de données KEGG pour déterminer quels gènes appartiennent à quelles voies biologiques ou processus.
3. **Évaluation de l'enrichissement :** On évalue si certains termes KEGG (voies métaboliques, fonctions cellulaires, etc.) sont sur-représentés parmi les gènes ou protéines d'intérêt par rapport à ce qui serait attendu au hasard.
4. **Interprétation biologique :** Les résultats de l'analyse d'enrichissement KEGG permettent d'interpréter biologiquement les données en mettant en évidence les voies biologiques ou les processus cellulaires qui sont pertinents pour le jeu de gènes ou de protéines.

Cela peut être particulièrement utile dans le domaine de la génomique fonctionnelle pour comprendre les processus biologiques sous-jacents à des expériences génétiques ou à des jeux de données d'expression génique. L'enrichissement KEGG fournit une perspective contextuelle en reliant les gènes ou protéines à des voies biologiques spécifiques, facilitant ainsi l'interprétation biologique des résultats expérimentaux.

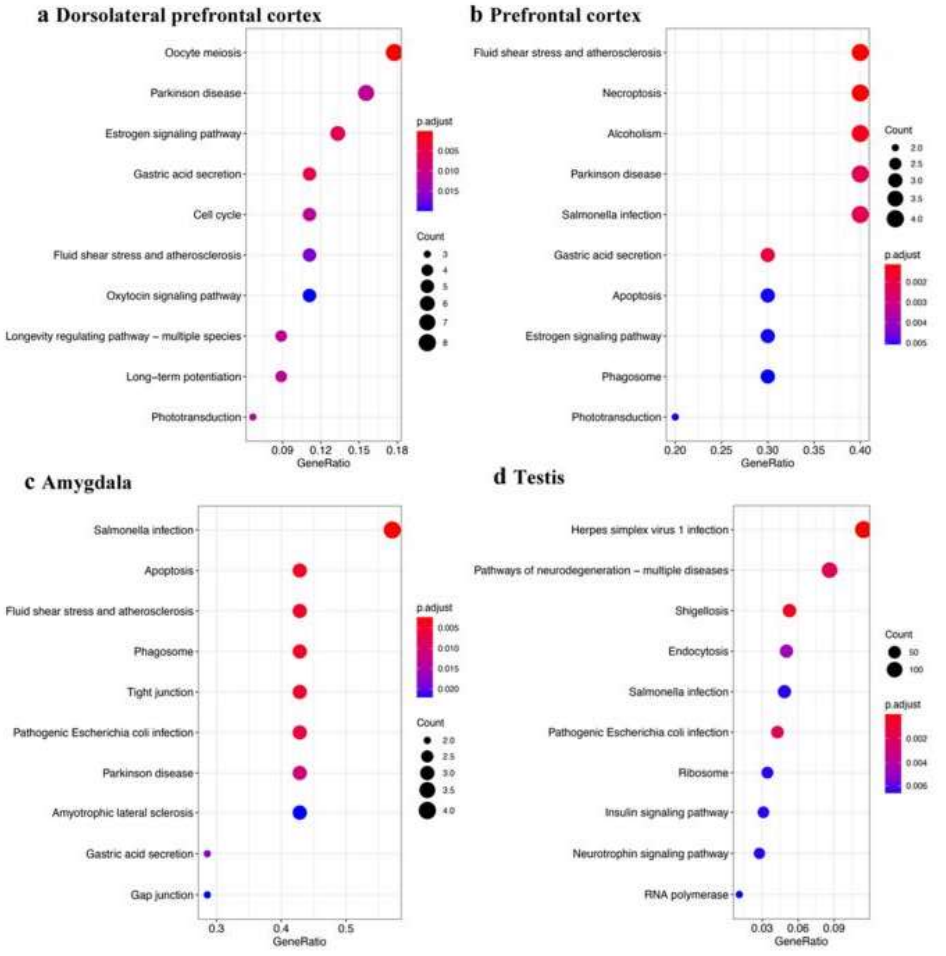


Figure 5. KEGG enrichment results for 3′UTR-piRNA alignment genes. KEGG enrichment analysis with protein-coding genes containing 3′UTR aligned by annotated piRNAs in brain tissues (**a**–**c**) and testis tissue (**d**). Gene ratio = Gene number in query list (piRNAs aligned in gene list)/Total gene number of specific pathway in database.

<= pas un mot?

reported the existence of pre-pachytene piRNAs derived from 3′UTR of protein-coding genes in germline cells [17]. To our surprise, both brain tissue and testis tissue achieve en-

reported the existence of pre-pachytene piRNAs derived from 3′UTR of protein-coding genes in germline cells [17]. To our surprise, both brain tissue and testis tissue achieve enrichment results for "Parkinson's disease" and "Pathways of Neurodegeneration–multiple diseases", respectively (Figure 5). However, the function of these sense-piRNAs is indistinct. They might be transacting with their derived mRNAs by an unknown mechanism. When

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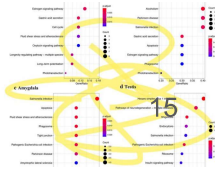
pathways of neuro: Description large, ont l'air de parler d'évènement racine commun à toutes les M ND. Soucis: présent nul part ailleurs, et malgré tout pas de piRNA parkinson dans les balls?
https://www.genome.jp/pathway/hsa05022

diseases", respectively (Figure 5). However, the function of these sense-piRNAs is indistinct. They might be transacting with their derived mRNAs by an unknown mechanism. When we used the transcript (including CDS, exon, 3′UTR, and 5′UTR) aligned by piRNAs to perform enrichment analysis of the three different brain tissues, testis, and ovary, all tissues identified an enrichment of neurodegeneration related genes.

Quand ils utilisent les transcrits provenant d'ailleurs 3 UTR, tous sont enrichis en neurodeg(...)

golo =>




ZMOONCHILD
We got this
Ah shit, here we go again.

Ah, d'accord, je vois où tu veux en venir. En génétique, le terme "cycle ping-pong" est souvent associé à la biogenèse des piARN (petits ARN interférents). Les piARN sont des molécules d'ARN qui jouent un rôle dans la régulation de l'expression génique.

Le cycle ping-pong des piARN implique une interaction entre deux populations de piARN, appelées piARN guides et piARN associés. Ces deux types de piARN interagissent avec des protéines impliquées dans le processus. Le cycle commence par le piARN guide qui s'associe à une protéine Argonaute et cible spécifiquement un ARNm complémentaire, entraînant la dégradation de l'ARNm cible.

Ensuite, le piARN associé, qui est produit à partir de l'ARNm cible dégradé, se lie également à une protéine Argonaute. Ce piARN associé peut à son tour cibler d'autres ARNm avec une séquence complémentaire, créant ainsi un "ping-pong" d'interactions entre les piARN guide et associés.

Ce cycle ping-pong permet d'amplifier la réponse silencieuse de l'ARNm, renforçant ainsi la régulation post-transcriptionnelle. C'est une sorte de mécanisme de défense cellulaire contre les éléments génétiques mobiles et peut également jouer un rôle dans d'autres processus biologiques.

ping pong time

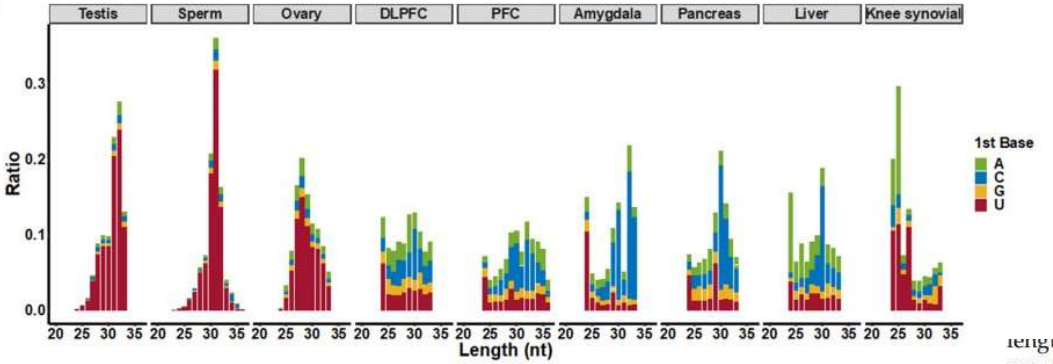


Figure 6. The length distribution of annotated piRNAs. The *y*-axis represents the ratio c reads with specific length/base to total annotated piRNAs reads in that tissue. Colors repr first base of annotated piRNAs.

length features. Somatic piRNAs show shorter and more evenly distributed lengths than germline piRNAs (Figure 6). According to the ping-pong cycle biogenesis pathway, tissues

length features. Somatic piRNAs show shorter and more evenly distributed lengths than germline piRNAs (Figure 6). According to the ping-pong cycle biogenesis pathway, tissues with significant ping-pong cycle signals synthesize piRNAs, which possess a 5′U bias and an A nucleotide bias at the 10th position. We found these attributes in testis, sperm, and ovary derived piRNAs from our analysis pipeline. However, we were not able to uncover evidence of ping-pong cycle biogenesis in somatic tissues based upon the distribution of mapped reads (Figure 6). We further confirmed this with an algorithm, pingpongpro [108], which also was not able to detect a ping-pong cycle signal in somatic tissues.

Résumé: Si un tissu a un signal de synthèse de piRNA en mode ping pong ils ont tendance à avoir en 5’ une base U et base A en 10th (?). C’est le cas en germinal, pas de pong-pong en somatique en revanche

3.2. piRNAs in Parkinson's Disease

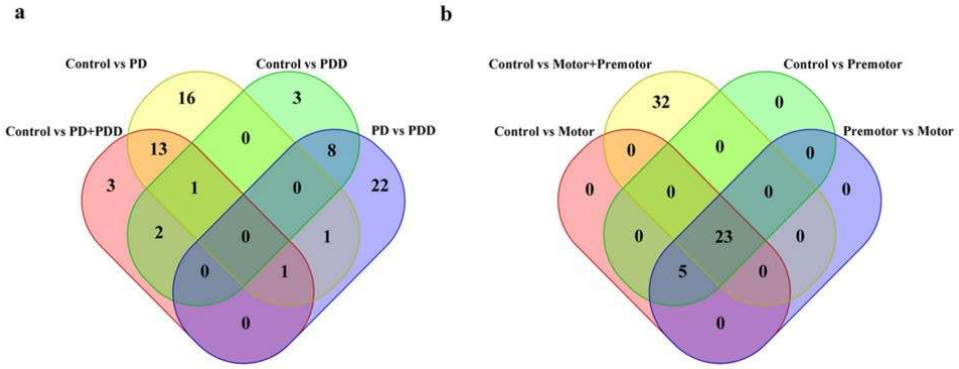


Figure 7. Venn plots of differently expressed piRNAs. Venn plots of differentially expressed piRNAs from prefrontal cortex (**a**) and amygdala (**b**). The Wilcoxon test was used to detect differently expressed piRNAs between different groups with p-value < 0.05. PD: Parkinson's disease; PDD: Parkinson's disease dementia.

précision erreur: PD+PDD et non PD significantly different pour coretex prefrontal

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Traduction post bleu: une méthode de prédiction a montré que les 55 piRNA surexprimé dans l'amygdale ciblent 20 protéines, dont plusieurs liées à M parkinson/neuro deg dans KEGG. par contre aucun de ces gènes ne sont ciblés par les piRNA surexprimés dans cortex.

significantly different in PD (Figure 7a). Among these, one piRNA (piR-hsa-748391) was expressed differently in PD in both prefrontal cortex and amygdala tissues. Unfortunately,

expressed differently in PD in both prefrontal cortex and amygdala tissues. Unfortunately, none of 3′UTR derived piRNAs from neurodegeneration-related genes mentioned above were among these differently expressed piRNAs. A target predicting method raised

To determine the significance of somatic piRNAs in human disease, we detected 296 piRNAs in the prefrontal cortex of which 20 piRNA expression levels were significantly different in PD; and 508 piRNAs in amygdala of which 55 piRNA expression levels were significantly different in PD (Figure 7a). Among these, one piRNA (piR-hsa-748391) was expressed differently in PD in both prefrontal cortex and amygdala tissues. Unfortunately, none of 3′UTR derived piRNAs from neurodegeneration-related genes mentioned above were among these differently expressed piRNAs. A target predicting method raised by a previous paper [109] showed 55 differently expressed piRNAs in amygdala target 20 proteins. Of these 20 proteins, MT-CO1 and MT-CO3 were included in the Parkinson's disease KEGG enrichment result, while MT-CO1, MT-CO3, and GRIA4 was included in the Pathways of neurodegeneration-multiple diseases KEGG enrichment result. However, this stringent target prediction method predicted that none of the genes were targeted by piRNAs differently expressed in PD prefrontal cortex.

We also found five piRNAs were differently expressed among the control, premotor stage PD, and motor stage PD in amygdala but not in the control vs. PD (premotor plus motor stage) (Figure 7b). Among these, piR-hsa-131693 is predicted to target MT-CO3 and MT-CO3 related pseudogenes (MT-CO3, MTCO3P12, MTCO3P18, MTCO3P8, MTCO3P38, MTCO3P7, MTCO3P13, and MTCO3P22) and the expression of piR-has-131693 decreases as PD disease progresses in amygdala. In the prefrontal cortex, we also identified different piRNAs expression patterns in PD and PDD, although there were no significant enrichment results with their predicted target genes (Figure 7a). In PD SEVs, we found 17 differently expressed piRNAs, of which piR-hsa-2435261 was predicted to target TANGO2 and piR-hsa-1516701 was predicted to target JAK3. In PD LEVs, two differently expressed piRNAs were detected with no specific predicted target genes.

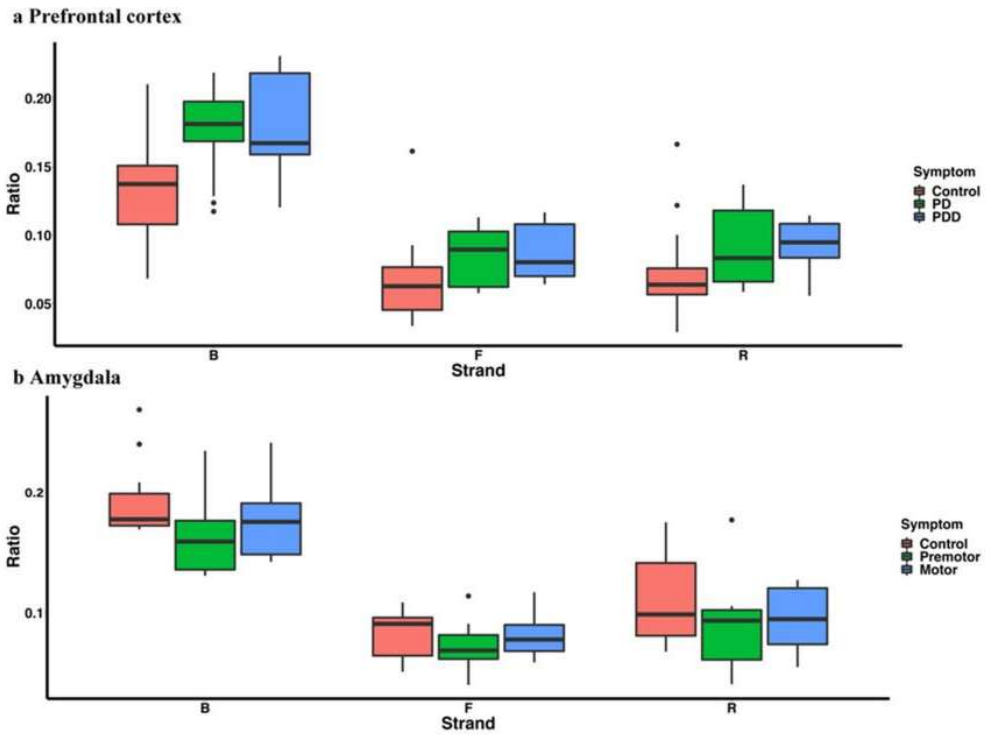

Figure 8. The percentage of annotated piRNAs reads mapped to transposons in prefrontal cortex (**a**) and amygdala (**b**) Ratio = reads number mapped to transposons (or subtypes)/total annotated piRNAs reads number.

We observed a higher percentage of transposon-derived piRNAs in the PD group in the prefrontal cortex (control vs. PD, control vs. PDD, control vs. PD plus PDD), but no significant difference between PD and PDD (Figure 8a). However, the transposon-

but no significant difference between PD and PDD (Figure 8a). However, the transposon-derived piRNA expression difference between PD and control in amygdala is not significant

(Figure 8b). In contrast, piRNAs in PD showed higher pseudogene alignment in the prefrontal cortex (Figure 9a), where the different piRNA-aligned pseudogenes were HSP90AA1 and EEF1A1-related pseudogenes. Interestingly, these two genes have been reported as

Pourcentage de piRNA mappé à des à des transposons (dérivé/dirigé vers?)