Parkinsonism

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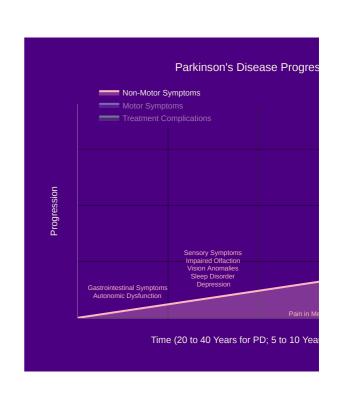
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Abstract

NOTE - this document is in draft currently. If I have the discipline, I will be making additions and edits for the next few months

Parkinsonism is a category of neurological diseases characterized by common mobility symptoms. Specific diseases include Parkinson's Disease (PD), Lewy Body Dementia (LBD), Progressive Supranuclear Palsy (PSP), and Multiple System Atrophy (MSA). These diseases have complex and heterogeneous pathologies that are not well understood. Common pathology attributes for idiopathic parkinsonism include misfolded proteins leading to toxic aggregates within the central nervous system (CNS), dysfunctional mitochondria resulting in impaired energy production and oxidative stress, chronic CNS inflammation, and dysfunctional cellular machinery that would otherwise correct misfolded protein conformation. The pathologies diverge based on which types of cells are affected, which protein aggregates, and which regions of the brain these changes occur.

Exosomes

Exosomes are small extracellular vesicles that play a key role in cell-to-cell communication and waste removal by transporting molecular cargo such as proteins, RNA, and lipids. Research within the last decade has focused on their potential in targeted therapy delivery, disease biomarker discovery, immune system modulation, and strategies to block their uptake to mitigate pathological processes. [Citation Needed]

Regarding neurodegenerative diseases, exosomes are being studied as potential biomarkers for early diagnosis, particularly for disorders like Parkinson's Disease and Multiple System Atrophy. [Citation Needed] These diseases have long prodromal phases, during which symptoms may be subtle or non-motor in nature, delaying diagnosis until neurodegeneration is already advanced. Since current diagnostic methods rely heavily on clinical evaluations of motor dysfunction, the identification of exosome-based biomarkers could enable earlier, more precise detection. Importantly, clinically viable biomarkers must be detectable in peripheral fluids such as blood or saliva, allowing for non-invasive testing during routine healthcare visits. This could shift the diagnostic paradigm from symptom-based assessments to proactive screening, potentially enabling earlier interventions that slow disease progression.

Importantly, exosomes can cross the blood-brain barrier (BBB) bidirectionally, [Citation Needed] allowing for the collection of CNS biomarkers in peripheral fluids and enabling potential therapeutic delivery to the brain. However, in neurodegenerative diseases, a compromised BBB may also permit the entry of exosomes carrying toxic cargo, potentially contributing to disease progression by spreading misfolded proteins, exacerbating neuroinflammation, and inducing metabolic stress. Additionally, exosomes can transport immune-modulating factors, such as cytokines or microRNA, which may further disrupt CNS homeostasis. Understanding these mechanisms is critical, as exosomes could serve as both pathological agents and therapeutic targets in neurodegenerative disease management. [Citation Needed]

Beyond their role in disease progression, exosomes also serve as natural concentrators of key biomarkers, which might otherwise be too dilute in peripheral fluids like blood or saliva for reliable detection. Furthermore, exosomes carry surface antigens reflective of their parent cells, allowing for selective isolation of disease-relevant exosomes. [Citation Needed] By isolating exosomes derived from specific cell types, such as dopaminergic neurons or oligodendrocytes, researchers can obtain enriched biomarker profiles in measurable concentrations, enhancing disease detection. This makes exosome-based diagnostics a promising avenue for the early identification and monitoring of neurodegenerative conditions.

This manuscript is a template (aka "rootstock") for Manubot, a tool for writing scholarly manuscripts. Use this template as a starting point for your manuscript.

The rest of this document is a full list of formatting elements/features supported by Manubot. Compare the input (`.md` files in the `/content` directory) to the output you see below.

Basic formatting

Bold text

Semi-bold text

<div align="center">Centered text</div>

<div align="right">Right-aligned text</div>

Italic text

Combined *italics and **bold***

~~Strikethrough~~

1. Ordered list item
2. Ordered list item
   a. Sub-item
   b. Sub-item
      i. Sub-sub-item
3. Ordered list item
   a. Sub-item

- List item
- List item
- List item

subscript: H_2O is a liquid

superscript: 2^{10} is 1024.

unicode superscripts^{0123456789}

unicode subscripts$_{0123456789}$

A long paragraph of text. Lorem ipsum dolor sit amet, consectetur adipiscing elit, sed do eiusmod tempor incididunt ut labore et dolore magna aliqua. Ut enim ad minim veniam, quis nostrud exercitation ullamco laboris nisi ut aliquip ex ea commodo consequat. Duis aute irure dolor in reprehenderit in voluptate velit esse cillum dolore eu fugiat nulla pariatur. Excepteur sint occaecat cupidatat non proident, sunt in culpa qui officia deserunt mollit anim id est laborum.

Putting each sentence on its own line has numerous benefits with regard to editing and version control.

Line break without starting a new paragraph by putting
two spaces at end of line.

Document organization

Document section headings:

Heading 1

Heading 2

Heading 3

Heading 4

Heading 5

Heading 6

A heading centered on its own printed page

Horizontal rule:

`Heading 1`'s are recommended to be reserved for the title of the manuscript.

`Heading 2`'s are recommended for broad sections such as *Abstract*, *Methods*, *Conclusion*, etc.

`Heading 3`'s and `Heading 4`'s are recommended for sub-sections.

Links

Bare URL link: https://manubot.org

Long link with lots of words and stuff and junk and bleep and blah and stuff and other stuff and more stuff yeah

Link with text

Link with hover text

Link by reference

Citations

Citation by DOI [1].

Citation by PubMed Central ID [2].

Citation by PubMed ID [3].

Citation by Wikidata ID [4].

Citation by ISBN [5].

Citation by URL [6].

Citation by alias [7].

Multiple citations can be put inside the same set of brackets [1,5,7]. Manubot plugins provide easier, more convenient visualization of and navigation between citations [2,3,7,8].

Citation tags (i.e. aliases) can be defined in their own paragraphs using Markdown's reference link syntax:

Referencing figures, tables, equations

Figure 1

Figure 2

Figure 3

Figure 4

Table 1

Equation 1

Equation 2

Quotes and code

> Quoted text

> Quoted block of text
>
> Two roads diverged in a wood, and I—
> I took the one less traveled by,
> And that has made all the difference.

Code `in the middle` of normal text, aka `inline code`.

Code block with Python syntax highlighting:

```python
from manubot.cite.doi import expand_short_doi

def test_expand_short_doi():
    doi = expand_short_doi("10/c3bp")
    # a string too long to fit within page:
    assert doi == "10.25313/2524-2695-2018-3-vliyanie-enhansera-copia-i-insulyatora-gypsy-na-sintez-ernk-
        modifikatsii-hromatina-i-svyazyvanie-insulyatornyh-belkov-vtransfetsirovannyh-geneticheskih-konstruktsiyah"
```

Code block with no syntax highlighting:

```
Exporting HTML manuscript
Exporting DOCX manuscript
Exporting PDF manuscript
```

Figures

Figure 1: A square image at actual size and with a bottom caption. Loaded from the latest version of image on GitHub.

Figure 2: An image too wide to fit within page at full size. Loaded from a specific (hashed) version of the image on GitHub.

Figure 3: A tall image with a specified height. Loaded from a specific (hashed) version of the image on GitHub.

Figure 4: A vector `.svg` image loaded from GitHub. The parameter `sanitize=true` is necessary to properly load SVGs hosted via GitHub URLs. White background specified to serve as a backdrop for transparent sections of the image. Note that if you want to export to Word (`.docx`), you need to download the image and reference it locally (e.g. `content/images/vector.svg`) instead of using a URL.

Tables

Table 1: A table with a top caption and specified relative column widths.

Bowling Scores	Jane	John	Alice	Bob
Game 1	150	187	210	105
Game 2	98	202	197	102
Game 3	123	180	238	134

Table 2: A table too wide to fit within page.

	Digits 1-33	Digits 34-66	Digits 67-99	Ref.
pi	3.14159265358979323846264338327950	28841971693993751058209749459230	78164062862089986280348253 4211706	`piday.org`
e	2.71828182845904523536028747135266	24977572470936999595749669 6762772	40766303535475945713821785 2516642	`nasa.gov`

Table 3: A table with merged cells using the `attributes` plugin.

	Colors	
Size	**Text Color**	**Background Color**
big	blue	orange
small	black	white

Equations

A LaTeX equation:

$$\int_0^\infty e^{-x^2} dx = \frac{\sqrt{\pi}}{2} \tag{1}$$

An equation too long to fit within page:

$$x = a + b + c + d + e + f + g + h + i + j + k + l + m + n + o + p + q + r + s + t \\ + u + v + w + x + y + z + 1 + 2 + 3 + 4 + 5 + 6 + 7 + 8 + 9 \tag{2}$$

Special

⚠ **WARNING** *The following features are only supported and intended for* `.html` *and* `.pdf` *exports. Journals are not likely to support them, and they may not display correctly when converted to other formats such as* `.docx`.

> **LINK STYLED AS A BUTTON**

Adding arbitrary HTML attributes to an element using Pandoc's attribute syntax:

> Manubot Manubot Manubot Manubot Manubot. Manubot Manubot Manubot Manubot. Manubot Manubot Manubot. Manubot Manubot. Manubot.

Adding arbitrary HTML attributes to an element with the Manubot `attributes` plugin (more flexible than Pandoc's method in terms of which elements you can add attributes to):

Manubot Manubot Manubot Manubot Manubot. Manubot Manubot Manubot Manubot. Manubot Manubot Manubot. Manubot Manubot. Manubot.

Available background colors for text, images, code, banners, etc:

`white` `lightgrey` `grey` `darkgrey` `black` `lightred` `lightyellow` `lightgreen` `lightblue` `lightpurple` `red` `orange` `yellow` `green` `blue` `purple`

Using the [Font Awesome](#) icon set:

✔ ? ★ ▲ ✖ ⋯

📜 **Light Grey Banner**
useful for *general information* - [manubot.org](#)

ⓘ **Blue Banner**
useful for *important information* - [manubot.org](#)

🚫 **Light Red Banner**
useful for *warnings* - [manubot.org](#)

References

1. **Sci-Hub provides access to nearly all scholarly literature**
    Daniel S Himmelstein, Ariel Rodriguez Romero, Jacob G Levernier, Thomas Anthony Munro, Stephen Reid McLaughlin, Bastian Greshake Tzovaras, Casey S Greene
    eLife (2018-03-01) https://doi.org/ckcj
    DOI: 10.7554/elife.32822 · PMID: 29424689 · PMCID: PMC5832410

2. **Reproducibility of computational workflows is automated using continuous analysis**
    Brett K Beaulieu-Jones, Casey S Greene
    Nature biotechnology (2017-04) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6103790/
    DOI: 10.1038/nbt.3780 · PMID: 28288103 · PMCID: PMC6103790

3. **Bitcoin for the biological literature.**
    Douglas Heaven
    Nature (2019-02) https://www.ncbi.nlm.nih.gov/pubmed/30718888
    DOI: 10.1038/d41586-019-00447-9 · PMID: 30718888

4. **Plan S: Accelerating the transition to full and immediate Open Access to scientific publications**
    cOAlition S
    (2018-09-04) https://www.wikidata.org/wiki/Q56458321

5. **Open access**
    Peter Suber
    MIT Press (2012)
    ISBN: 9780262517638

6. **Open collaborative writing with Manubot**
    Daniel S Himmelstein, Vincent Rubinetti, David R Slochower, Dongbo Hu, Venkat S Malladi, Casey S Greene, Anthony Gitter
    Manubot (2020-05-25) https://greenelab.github.io/meta-review/

7. **Opportunities and obstacles for deep learning in biology and medicine**
    Travers Ching, Daniel S Himmelstein, Brett K Beaulieu-Jones, Alexandr A Kalinin, Brian T Do, Gregory P Way, Enrico Ferrero, Paul-Michael Agapow, Michael Zietz, Michael M Hoffman, ... Casey S Greene
    Journal of The Royal Society Interface (2018-04) https://doi.org/gddkhn
    DOI: 10.1098/rsif.2017.0387 · PMID: 29618526 · PMCID: PMC5938574

8. **Open collaborative writing with Manubot**
    Daniel S Himmelstein, Vincent Rubinetti, David R Slochower, Dongbo Hu, Venkat S Malladi, Casey S Greene, Anthony Gitter
    PLOS Computational Biology (2019-06-24) https://doi.org/c7np
    DOI: 10.1371/journal.pcbi.1007128 · PMID: 31233491 · PMCID: PMC6611653