Dihydropyrimidinase-like 2 (DPYSL2) regulates breast cancer migration via a JAK/STAT3/vimentin axis

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Research Paper Sections:

The sections of the research paper input text parsed in this audit.

Section No.	Headings	Sentences
Section: 1	Abstract	10
Section: 2	Introduction	17
N/A		0

Dihydropyrimidinase-like 2 (DPYSL2) regulates breast cancer migration via a JAK/STAT3/vimentin axis

cancer migration via a JAK/STAT3/vimentin axis

S1 [002] The intricate neuronal wiring during development requires cytoskeletal reorganization orchestrated by signaling cues.

The intricate neuronal wiring ...

- ... during development requires cytoskeletal reorganization orchestrated ...
- ... by signaling cues.

Abstract

S1 [001]

S1 [003] Considering that cytoskeletal remodeling is a hallmark of cell migration, we inquired whether metastatic cancer cells exploit the axon guidance proteins to migrate.

Considering ...

- ... that cytoskeletal remodeling is a hallmark ...
- ... of cell migration, ...
- ... we inquired ...
- ... whether metastatic cancer cells exploit the axon guidance proteins ...
- ... to migrate.
- **S1 [004]** Indeed, in breast cancer patients, we found a significant correlation between the mesenchymal markers and the expression of dihydropyrimidinase-like 2 (DPYSL2), a regulator of cytoskeletal dynamics in growing axons.

Indeed, ...

- ... in breast cancer patients, ...
- ... we found a significant correlation ...
- ... between the mesenchymal markers ...
- ... and the expression ...
- ... of dihydropyrimidinase-like 2 ...
- ... (DPYSL2), ...
- ... a regulator ...
- ... of cytoskeletal dynamics ...
- ... in growing axons.
- **S1 [005]** Strikingly, DPYSL2 knockout in mesenchymal-like cells profoundly inhibited cell migration, invasion, stemness features, tumor growth rate, and metastasis.

Strikingly, ...

- ... DPYSL2 knockout ...
- ... in mesenchymal-like cells profoundly inhibited cell migration, ...
- ... invasion, ...
- ... stemness features, ...
- ... tumor growth rate, ...
- ... and metastasis.

S1 [006] Next, we aimed to decode the molecular mechanism underlying this phenomenon and revealed an interaction between DPYSL2 and Janus kinase 1 (JAK1).

```
Next, ...
... we aimed ...
... to decode the molecular mechanism underlying this phenomenon ...
... and revealed an interaction ...
... between DPYSL2 ...
... and Janus kinase 1 ...
... (JAK1).
```

S1 [007] This binding is crucial for triggering signal transducer and activator of transcription 3 (STAT3) and subsequently expressing vimentin, the pro-migratory intermediate filament.

```
This binding is crucial ...
... for triggering signal transducer ...
... and activator ...
... of transcription 3 ...
... (STAT3) ...
... and subsequently expressing vimentin, ...
... the pro-migratory intermediate filament.
```

S1 [008] Collectively, we identified DPYSL2 as a molecular link between oncogenic signaling pathways and cytoskeletal reorganization in migrating breast cancer cells.

```
Collectively, ...
... we identified DPYSL2 ...
... as a molecular link ...
... between oncogenic signaling pathways ...
... and cytoskeletal reorganization ...
... in migrating breast cancer cells.
```

S1 [009] Statement of significance This study shows that the axon guidance adaptor protein DPYSL2 is essential for promoting breast cancer migration.

```
Statement ...
... of significance This study shows ...
... that the axon guidance adaptor protein DPYSL2 is essential ...
... for promoting breast cancer migration.
```

S1 [010] Specifically, this protein interacts with JAK1 to govern STAT3 signaling and subsequently vimentin expression.

```
Specifically, ...
... this protein interacts ...
... with JAK1 ...
... to govern STAT3 signaling ...
... and subsequently vimentin expression.
```

S2 [012] The guidance of developing neurons to their specific target region is regulated by a combination of signaling cues composed of ligand/receptor interactions (1).

```
The guidance ...
... of developing neurons ...
... to their specific target region is regulated ...
... by a combination ...
... of signaling cues composed ...
... of ligand/receptor interactions ...
... (1).
```

S2 [013] The axon guidance machinery includes distinct families of canonical guidance proteins, such as slit guidance ligand (SLIT) (2).

```
The axon guidance machinery includes distinct families ... ... of canonical guidance proteins, ... ... such as slit guidance ligand ... ... (SLIT) ... ... (2).
```

S2 [014] This family of secreted factors induces changes in the newly developing axon through interaction with members of the roundabout guidance receptor (ROBO) family (3).

```
This family ...
... of secreted factors induces changes ...
... in the newly developing axon ...
... through interaction ...
... with members ...
... of the roundabout guidance receptor ...
... (ROBO) ...
... family ...
... (3).
```

S2 [015] Other axon guidance families include the semaphorins and their receptors, neuropilins (NRP) (4).

```
Other axon guidance families include the semaphorins ...
... and their receptors, ...
... neuropilins ...
... (NRP) ...
... (4).
```

S2 [016] The outcome of semaphorins/NRP and ROBO/SLIT activation is structural reorganization of the cell (5) mediated by cytoskeleton binding proteins (6), such as the collapsin response mediator protein (CRMP) family (7).

```
The outcome ...
... of semaphorins/NRP ...
... and ROBO/SLIT activation is structural reorganization ...
... of the cell ...
... (5) ...
... mediated ...
... by cytoskeleton binding proteins ...
```

```
... (6), ...
... such as the collapsin response mediator protein ...
... (CRMP) ...
... family ...
... (7).
```

S2 [017] Thus, in development cytoskeletal rearrangement is a central process, which is necessary for the axons to navigate to their defined targets.

```
Thus, ...
... in development cytoskeletal rearrangement is a central process, ...
... which is necessary ...
... for the axons ...
... to navigate ...
... to their defined targets.
```

S2 [018] Epithelial-mesenchymal transition (EMT) was initially described as an early developmental program used by epithelial cells to trans-differentiate and gain mesenchymal-like properties (8).

```
Epithelial-mesenchymal transition ...
... (EMT) ...
... was initially described ...
... as an early developmental program used ...
... by epithelial cells ...
... to trans-differentiate ...
... and gain mesenchymal-like properties ...
... (8).
```

S2 [019] In tumors, this program is assumed to be the mechanism by which carcinomas gain aggressive features such as migratory capabilities, chemoresistance, and stemness (9-11).

```
In tumors, ...
... this program is assumed ...
... to be the mechanism ...
... by which carcinomas gain aggressive features ...
... such as migratory capabilities, ...
... chemoresistance, ...
... and stemness ...
... (9-11).
```

S2 [020] The activation of the EMT program by extracellular cues (12), such as the transforming growth factor- β (TGF β) (13,14) and interleukin 6 (IL-6) (9), results in significant transcriptome changes.

```
The activation ... ... of the EMT program ... ... by extracellular cues ... ... (12), ... ... such as the transforming growth factor-\beta ... ... (TGF\beta) ... ... (13,14) ... ... and interleukin 6 ... ... (IL-6) ...
```

End of Sample Audit

This is a truncated Manuscript Microscope Sample Audit.

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