

**Table S9.** Pathways associated with SEGS123 and common to the L and H1 isochore families.

| Pathways                                  | Accession <sup>1</sup> | References                            |
|-------------------------------------------|------------------------|---------------------------------------|
| General transcription by RNA polymerase I | P00022                 | (Grummt 2010; Pelletier et al., 2018) |
| Interleukin signaling pathway             | P00036                 | (Wang et al., 2024)                   |
| Ornithine degradation                     | P02758                 | (Liu et al., 2019)                    |
| Xanthine and guanine salvage pathways     | P02788                 | (Camici et al., 2019)                 |

<sup>1</sup> Pathway map accession number (replace X by the corresponding accession number in <https://www.pantherdb.org/pathway/pathwayDiagram.jsp?catAccession=X> to access the related pathway map).

#### *Contextualization of Table S9 information*

As the isochore classification of genes was based on the partition of their GC3 distribution, it is evident that this approach is imprecise, and consequently, some genes may be associated with two families. Therefore, we have listed in Table S9 the four pathways that were common to both L and H1 isochore families. To make this table more informative, we compiled and briefly summarized the quotations from its publication references as presented below.

Considering these pathways, cancer cells depend on persistent ribosome biogenesis by up-regulating Pol I transcription that is the rate-limiting step of ribosome biogenesis to match their increased proliferative and biosynthetic activity (Grummt, 2010)□. Stroma impacts tumor development through tumor-infiltrated immune cells that collectively maintain an inflammatory environment. This environment enables tumor growth and immune suppression during tumor progression. Inflammation-targeted agents have the potential to suppress cancer development and to improve the efficacy of other therapeutic agents. Interleukin (IL)-1 is upregulated in multiple tumor types. Positive correlations were identified between IL-1 $\beta$  expression and the infiltration of immunosuppressive myeloid-derived suppressor cells, as well as the expression of their chemoattractants in patients with K-ras-mutant lung adenocarcinoma (Wang et al., 2024). Ornithine aminotransferase promoted the proliferation and metastasis of non-small cell lung cancer via upregulation of miR-21 (Liu et al., 2019)□. The salvage pathway enzymes seem to play the key role in replenishing the purine pool in dividing and tumour cells that require a greater amount of nucleotides. Hypoxanthine-guanine phosphoribosyltransferase is an enzyme,

among others, involved in the purine metabolism of malignant cells whose modulation may affect the apoptotic programme (Camici et al., 2019)□.

## References

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