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Transcriptome and Proteome Analyses Reveal Stage-Specific DNA Damage Response in Embryos of Sturgeon (*Acipenser ruthenus*)

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Article

Ancient Sturgeons Possess Effective DNA Repair Mechanisms: Influence of Model Genotoxicants on Embryo Development of Sterlet, *Acipenser ruthenus*

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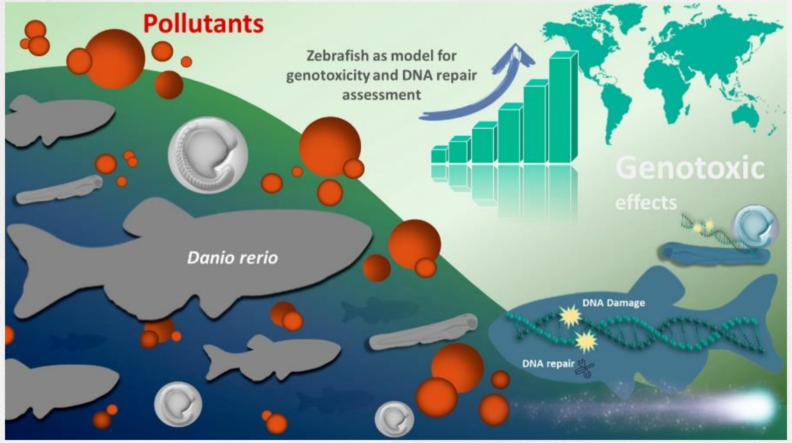
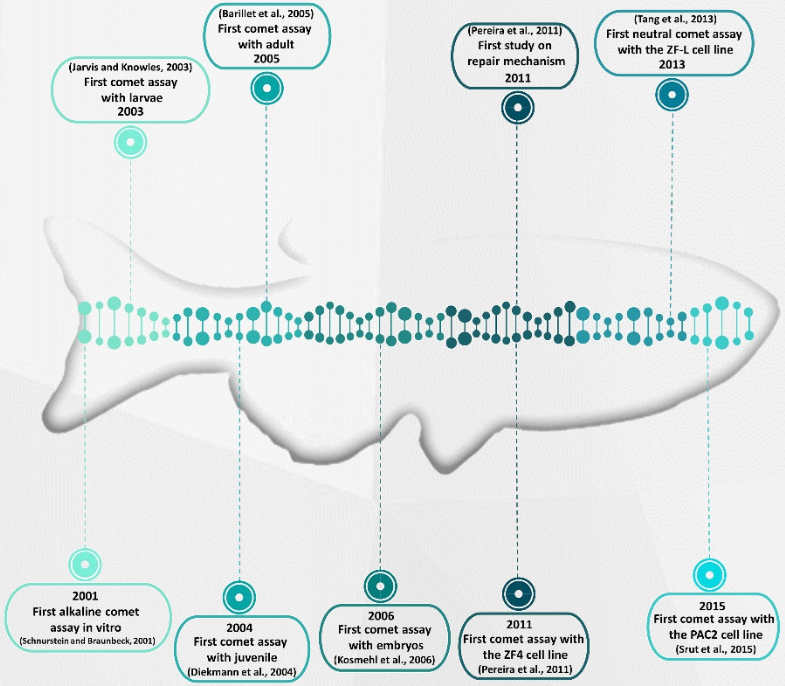
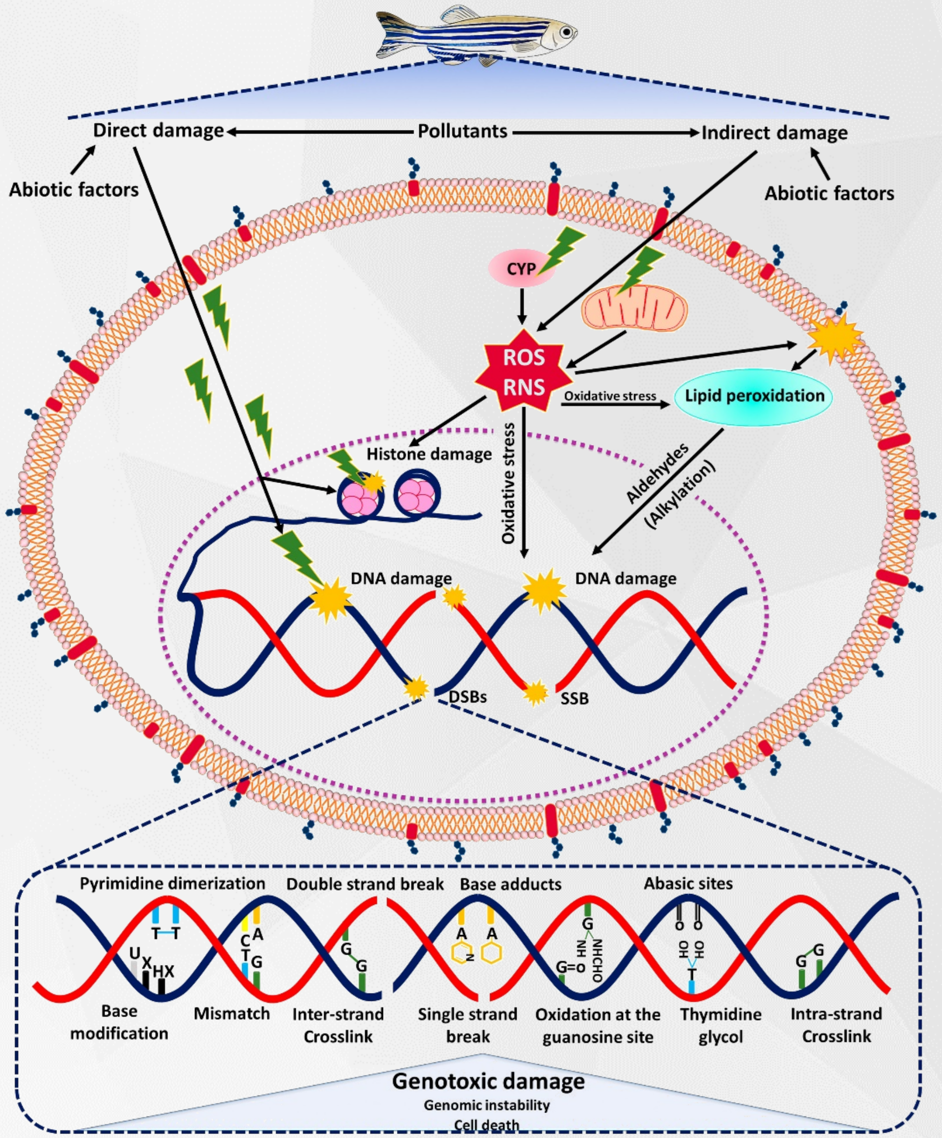
DNA repair genes play a variety of roles in the development of fish embryos

Abhipsha Dey, Martin Flajšhans, Martin Pšenička and Ievgeniia Gazo*

Background-Genotoxicity (Zebrafish)







Canedo & Rocha (2021). https://doi.org/10.1016/j.scitotenv.2020.144084

Background-DNA Damage Response

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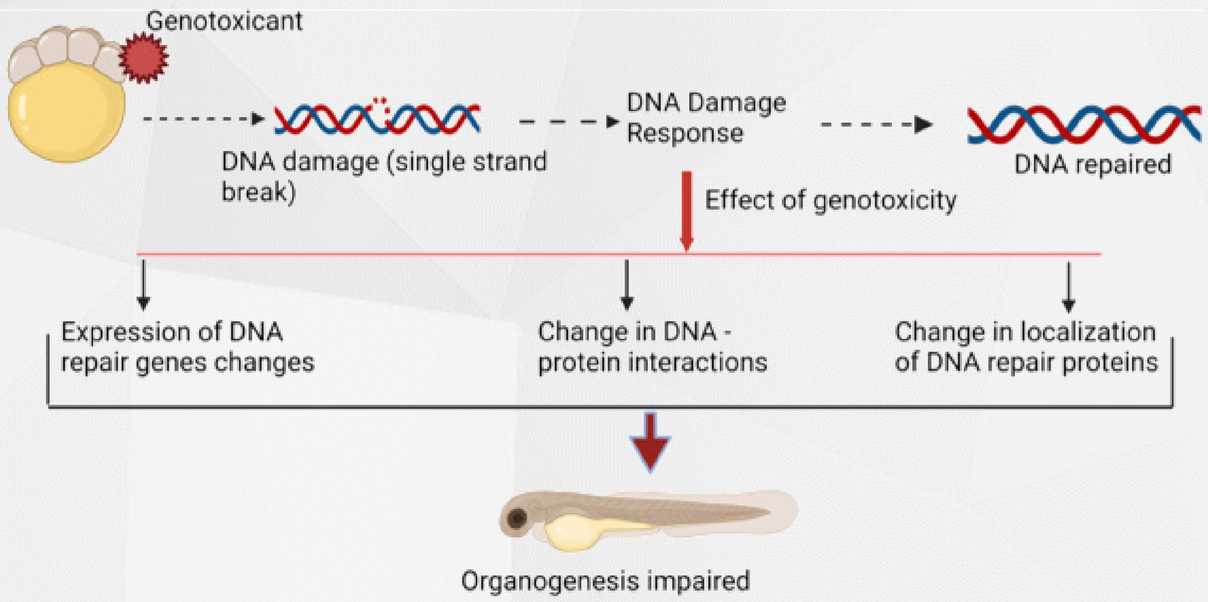

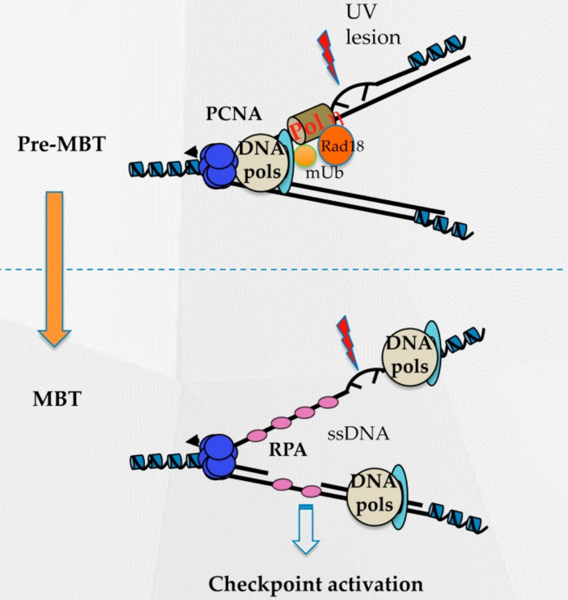

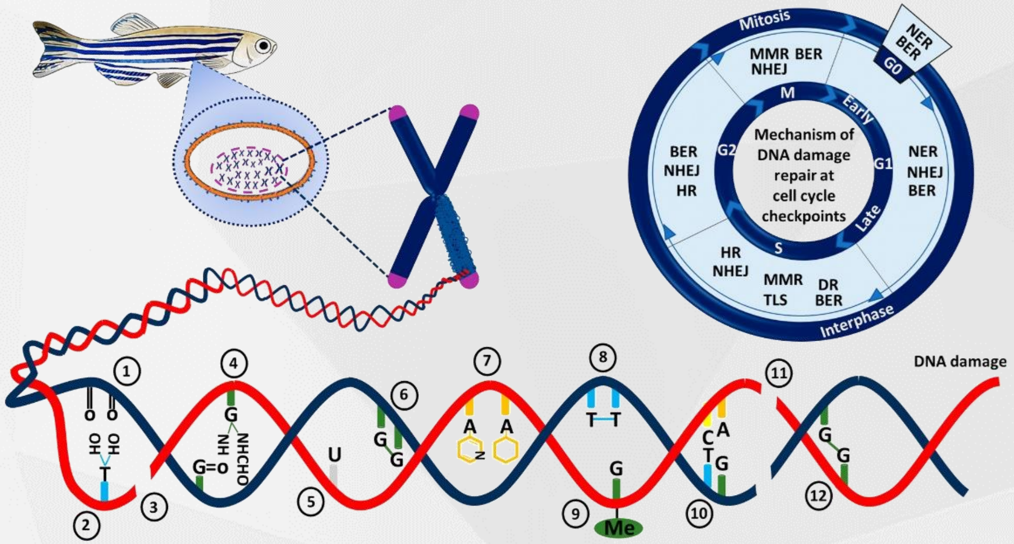

Agents	Ionizing radiation Aquilating agents ROS spontaneous reactions	UV-radiation Polycyclic aromatic hydrocarbons Carcinogenic agents ROS	UV-radiation	UV-radiation	Replication errors	UV-radiation ionizing radiation, alkylating agents ROS	UV-radiation ionizing radiation, alkylating agents ROS	Unrepaired DNA lesions
DNA damage	(1), (2), (3), (4), and (5)	(6), (7), and (8)	(8)	(4), (8), and (9)	(10)	(11) and (12)	(11) and (12)	(1) and (8)
Main repair pathway	BER	NER	PER	DR	MMR	HR	NHEJ	TLS
Main genes	apex1, polb, creb1, ogg1 and p53	xpc, xpd, xpa, xpf, p53, p21, ddb2, gadd45a, ciclinaG1 and vitelogenina	cry5	mgmt and o phr	msh2, msh6, mlh1, mlh2 and mlh6	reca, rad52, rad51 and rpa	dna-pk, xrcc5, ku80, xrcc6, ku70, zfl2-2, arte and ligIV	*poleta, poliota, polkappa, pollambda, polmu, polnu, rev1 and polzeta*
Damage recognition	DNA glycosylases	GGR: Xpc, Ddb2; TCR: Csa, Csb	photolyase; MTHF or 8-HDF; FADH⁻	mgmt	MSH2, MSH6 or MSH3, MSH2	MRE11, NBS1, RAD50	Ku70, Ku80	
Lesion excision	AP Endonuclease 1 (Apex1)	Xpa, Xpd and Xpg	No cleavage occurs	No cleavage occurs	MutLα (MLH1/PMS2) Endonuclease 1 (EXO1)	RPA, ATRIP and recombinase RAD51	DNA-PKCS	
DNA repair synthesis	DNA polymerase β	DNA polymerase β			DNA polymerase δ	DNA polymerase δ	Artemis, polymerase μ and λ, TDP1 or PNK	DNA polymerases of the Y family
DNA ligation	XRCC1/LIG3α	DNA ligase I and XRCC1/LIG3α			DNA ligase I	DNA ligase	IV/XRCC4 ligase	

Background-Sterlet (*Acipenser ruthenus*)

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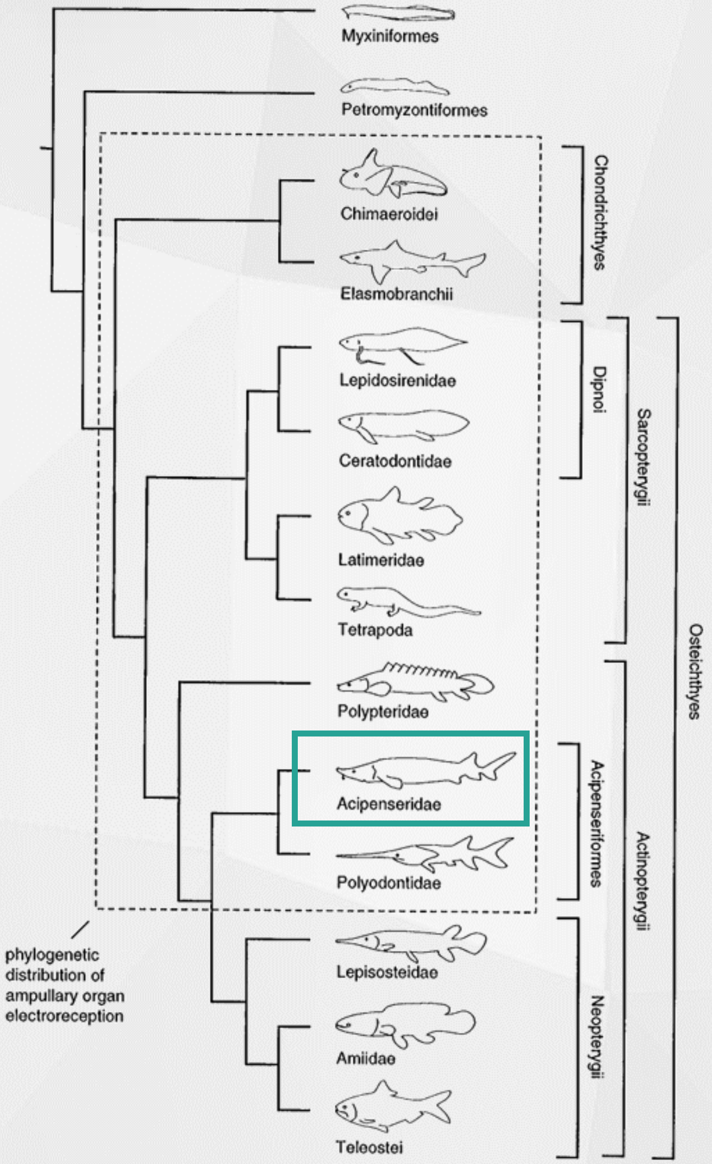
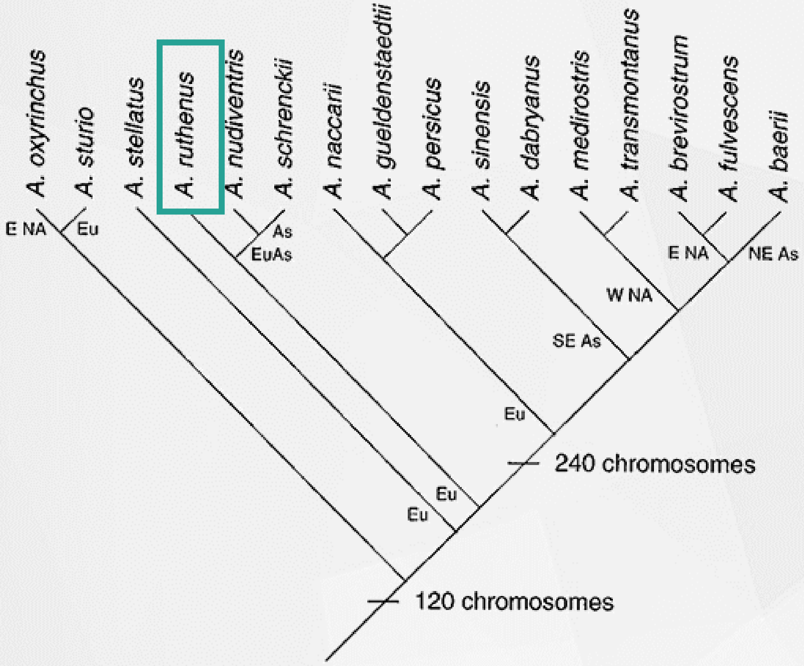
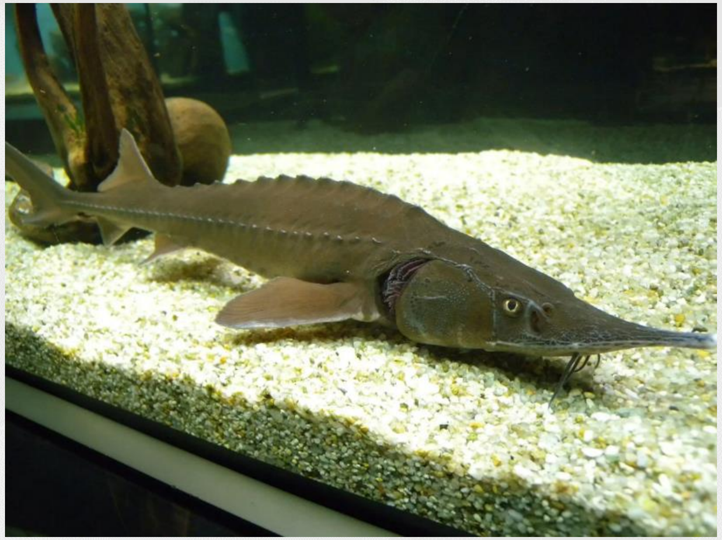
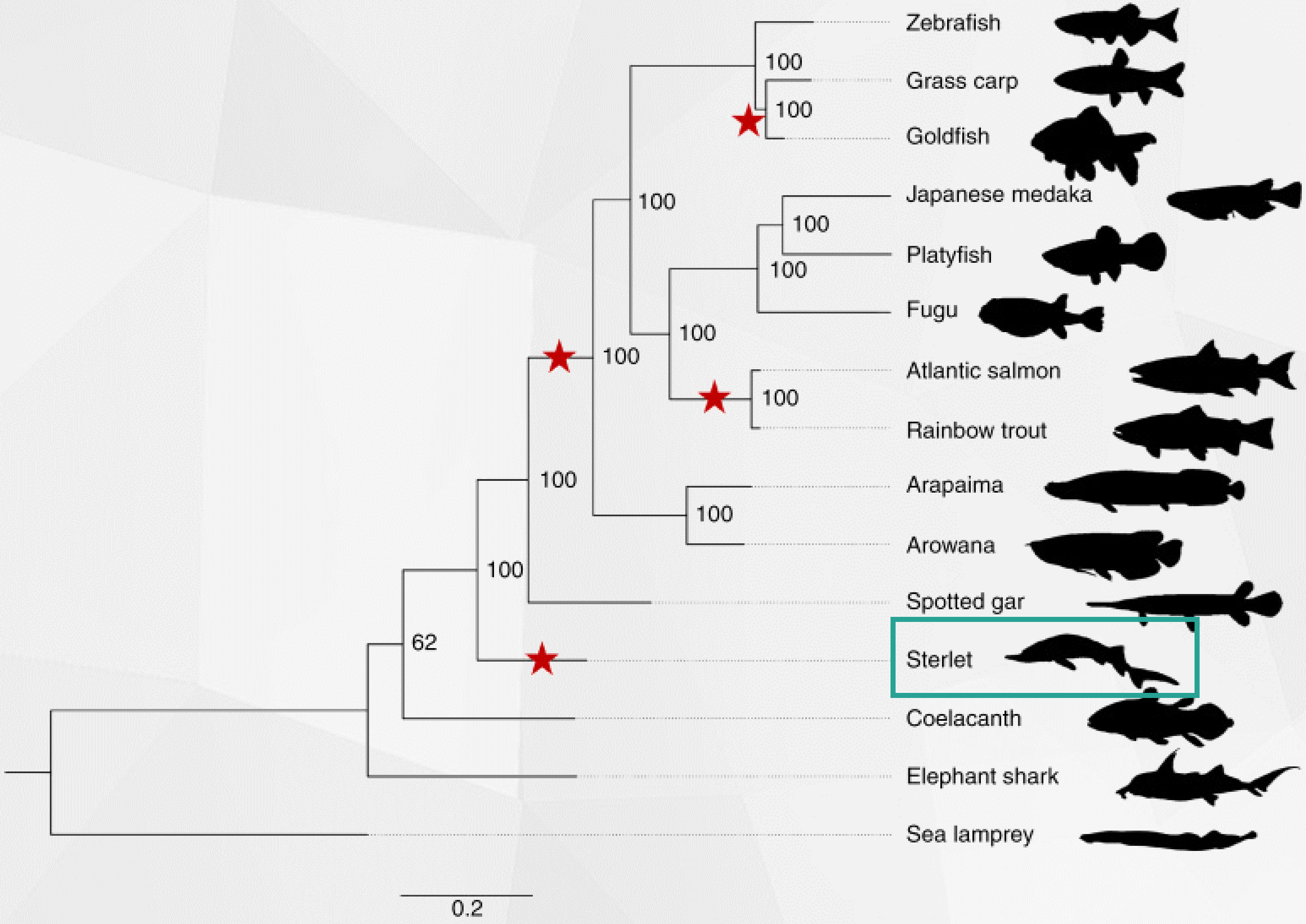
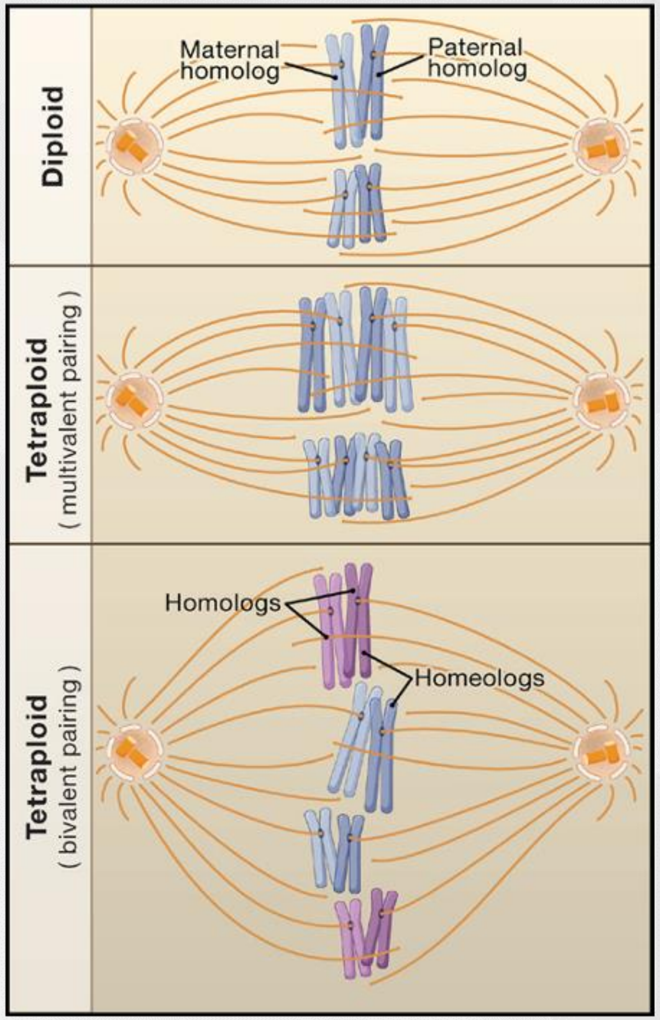






Background-Genomic Plasticity





Aim and Objective

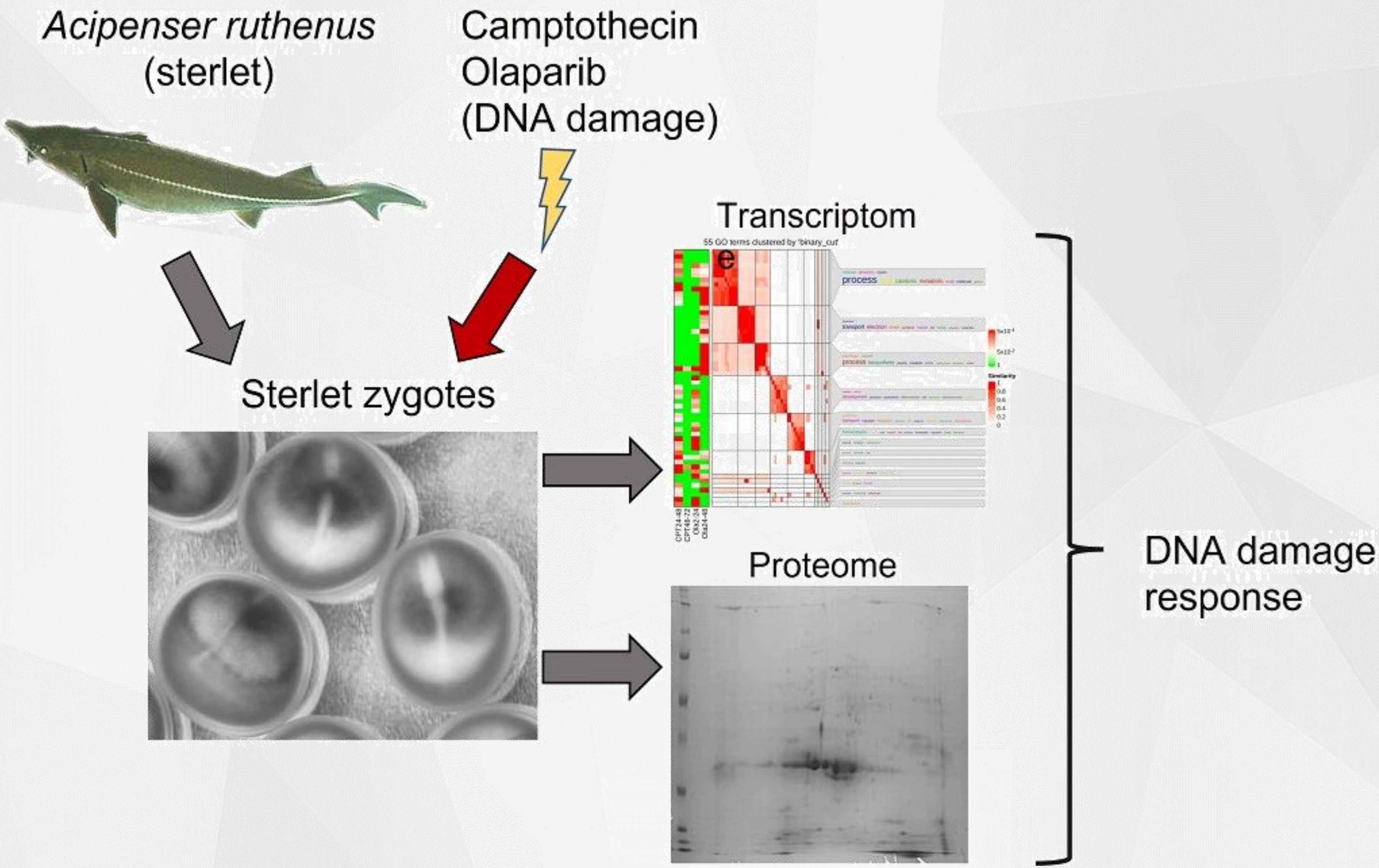
Objective:

- To investigate how genotoxicants affect the DNA damage response at different embryonic stages in *Acipenser ruthenus*.
- What are the transcriptomic and proteomic changes in response?

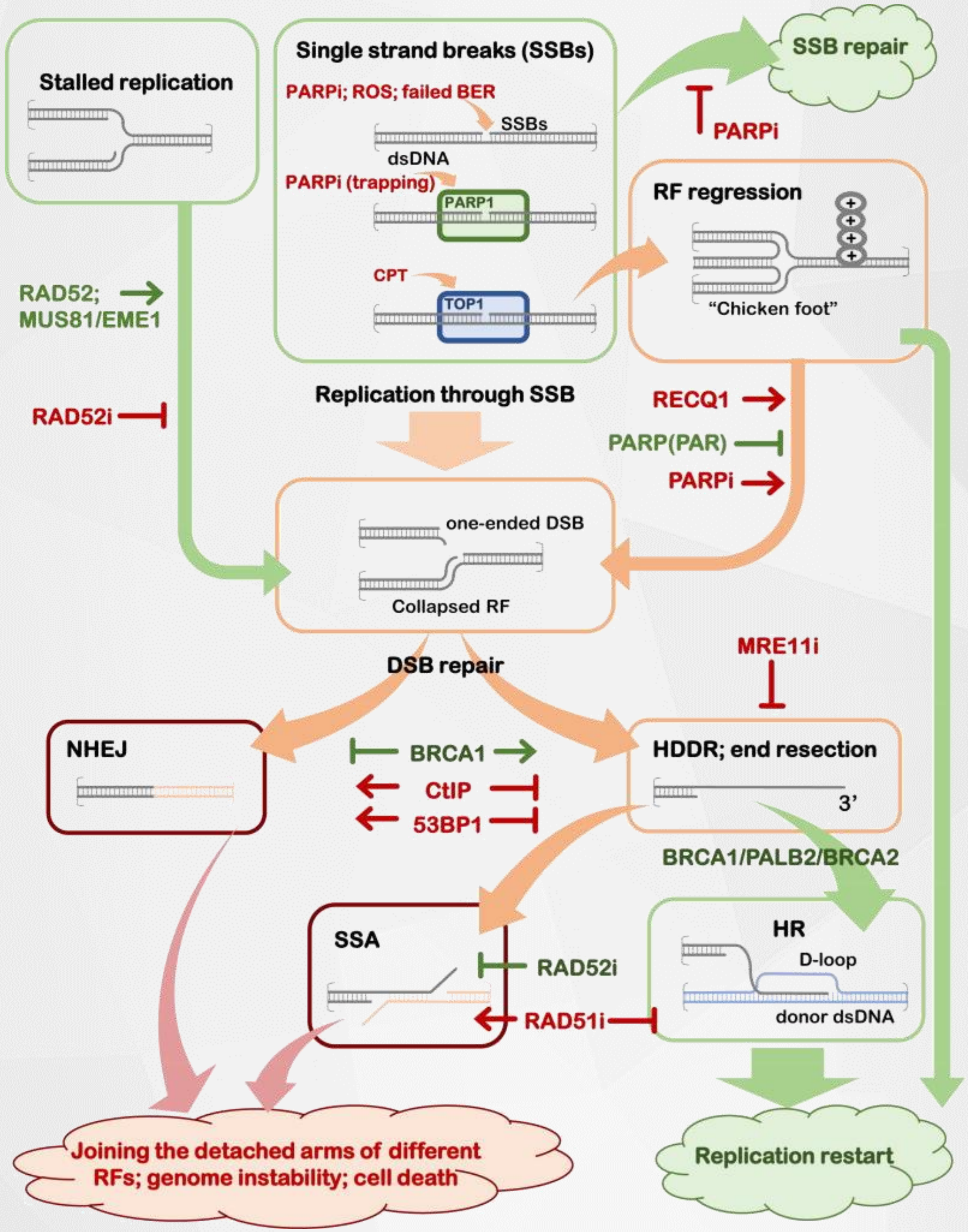
Genotoxicants tested:

- Camptothecin (CPT): Topoisomerase I inhibitor, induces DNA breaks.
- Olaparib (Ola): PARP-1 inhibitor, induces DNA damage.

Graphic Abstract



Principle



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Methods

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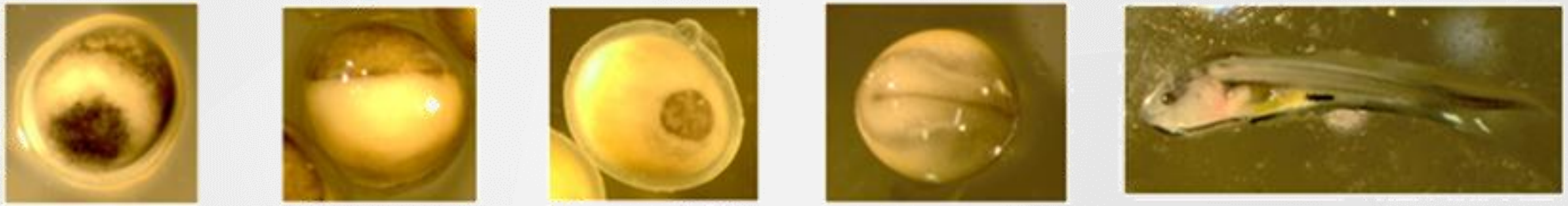
	blastula	mid-gastrula	late-gastrula	neurula	larva
Stages					
Hours post-fertilization (hpf)	2-24 hpf	24-48 hpf		48-72 hpf	Hatching (8 dpf)

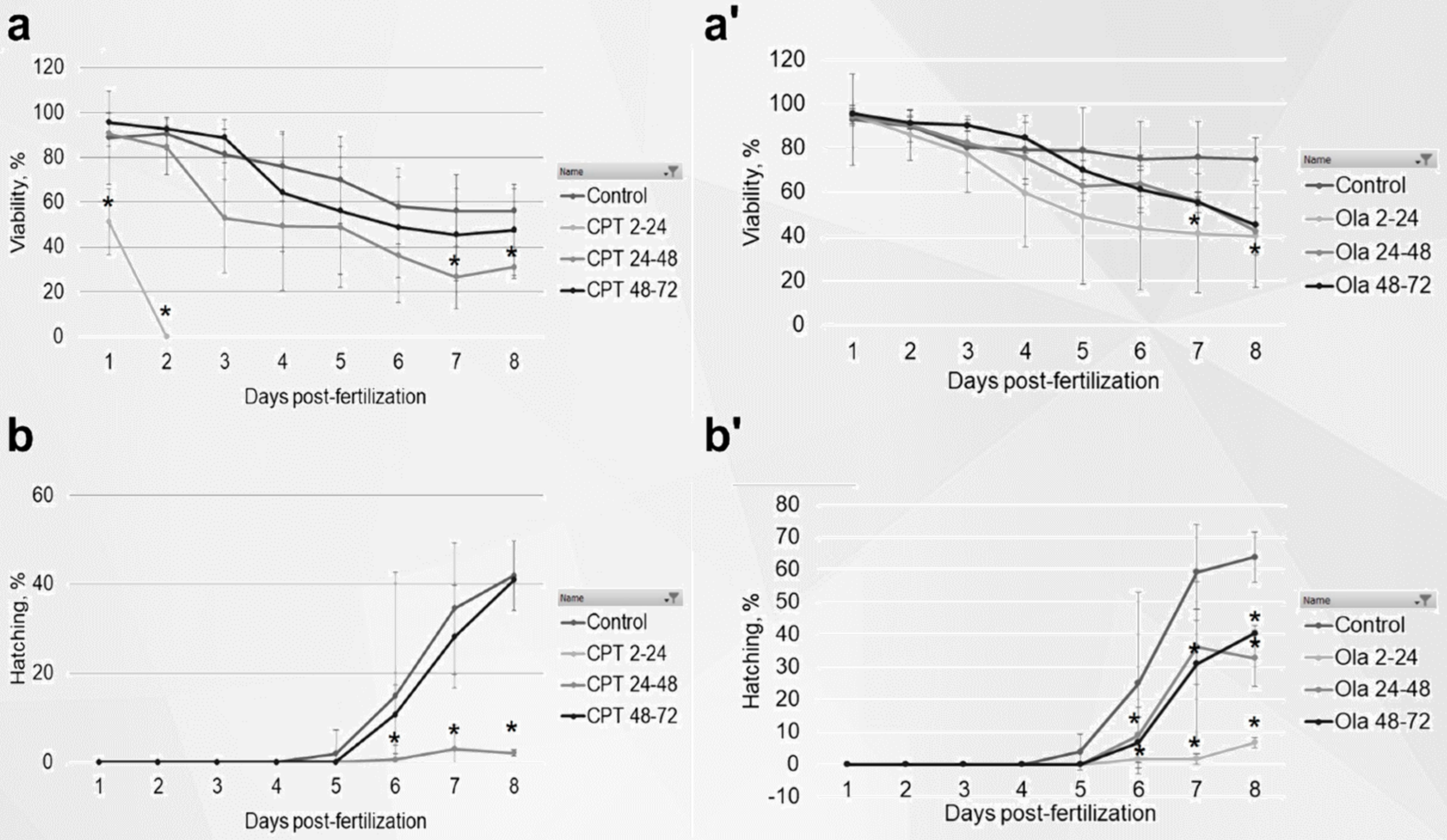


Fertilized embryos at 2-cell stage

7 nM CPT or 20 μM Ola

Result-Embryo Viability

- CPT/Ola exposure caused reduced viability and hatching rates, particularly at early stage.
- Later-stage exposure showed better survival and hatching.



Results-DNA Fragmentation

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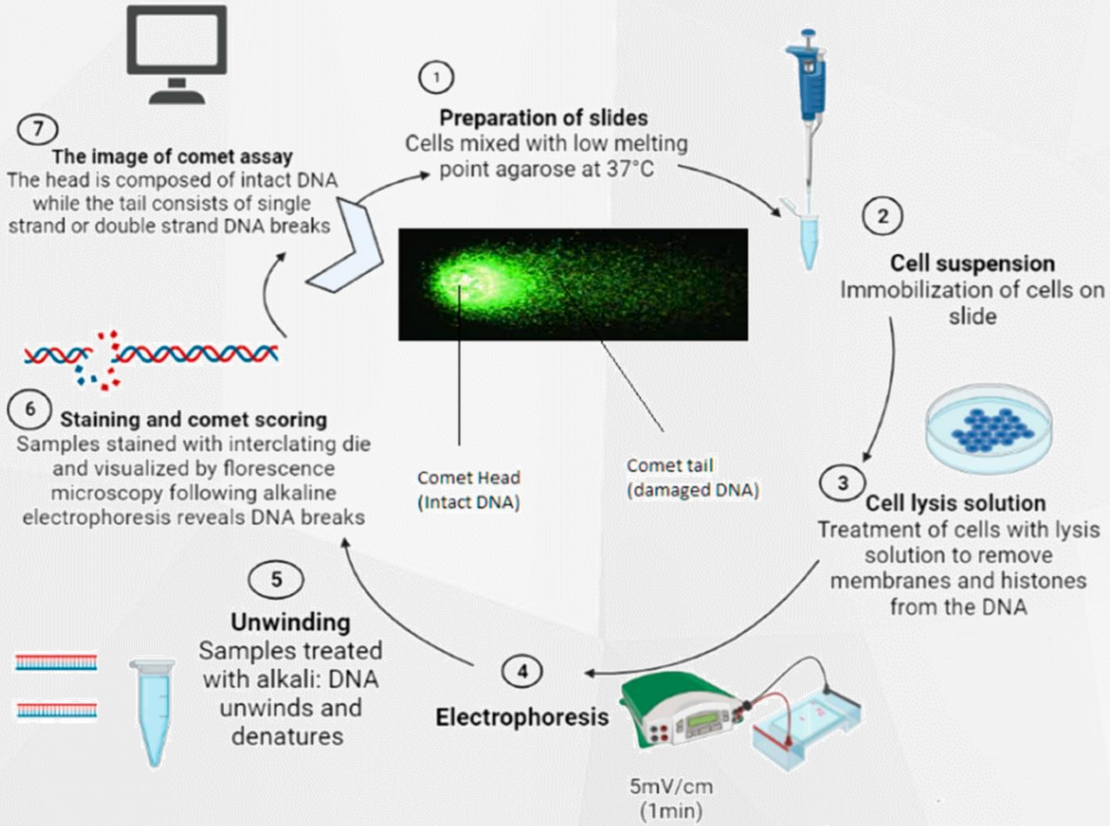
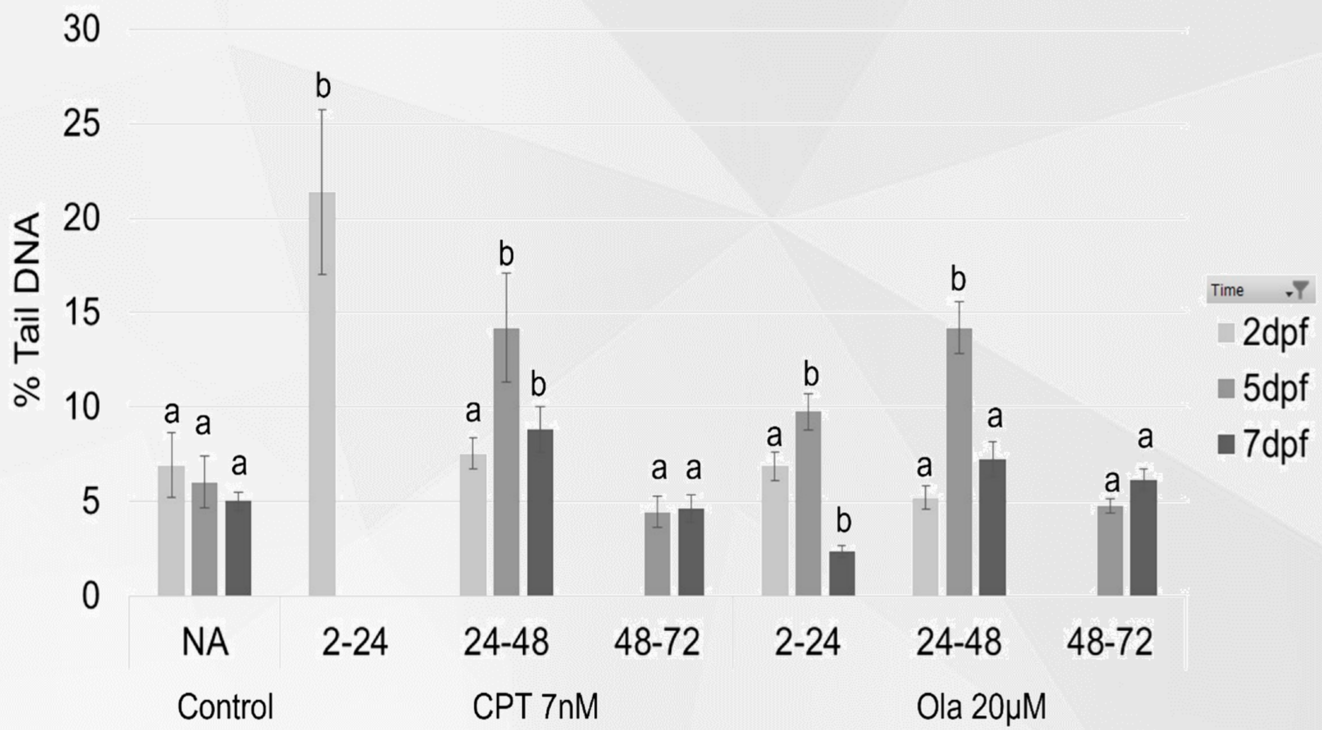
- Early-stage exposure to CPT/Ola caused increased DNA fragmentation.
- Later-stage exposure showed no effects.
- DNA repair occurs at 7 dpf.





Result-Phenotype Formation

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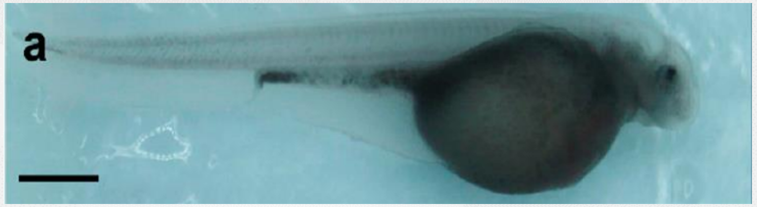
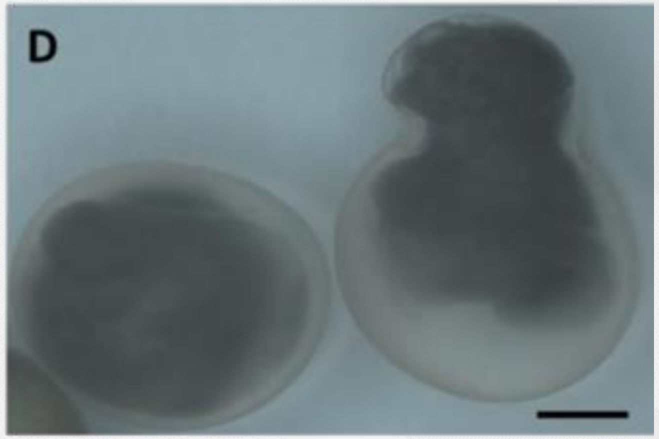
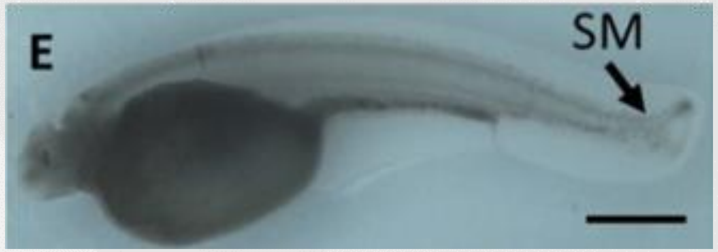
Control



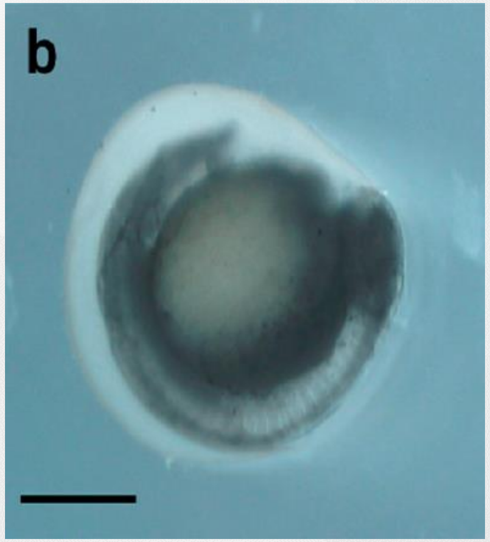
CPT 24-48



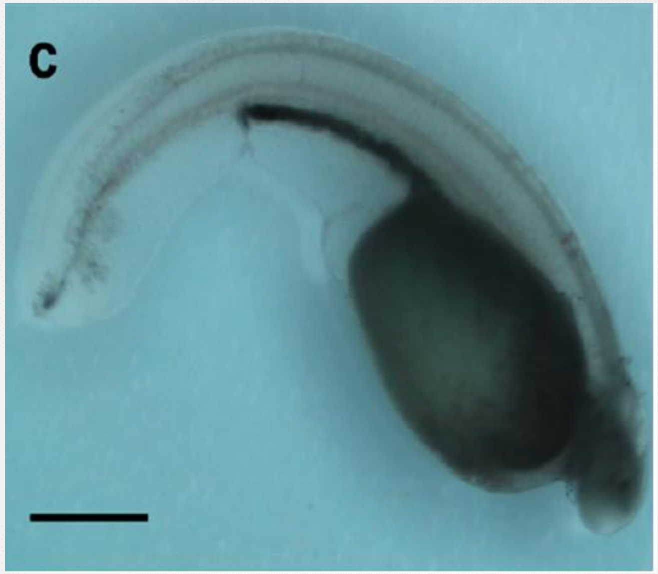
CPT 48-72



Ola 2-24



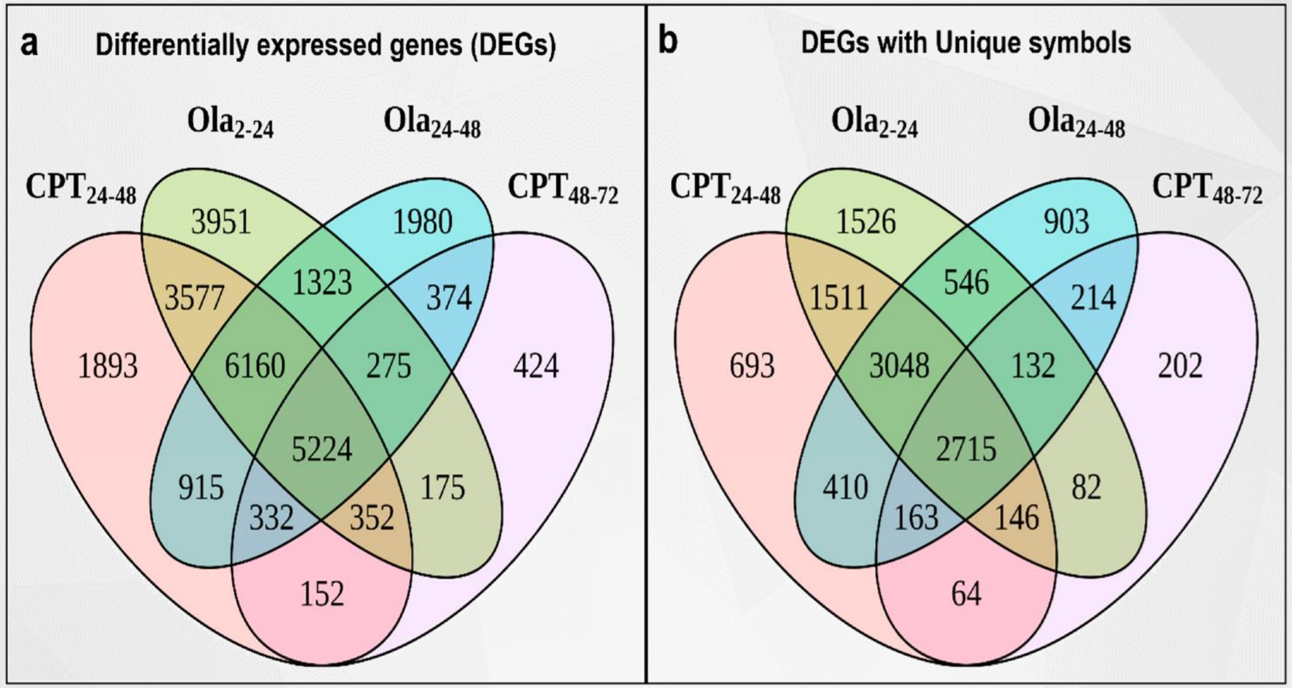
Ola 24-48



Ola 48-72

Result-Transcriptomic Patterns

- Overlapping DEGs: High overlap between CPT 24–48 hpf and Ola 2–24 hpf (56%).
- Stage-Specific Changes: Expression patterns varied by exposure stage.



Result-DDR Pathways

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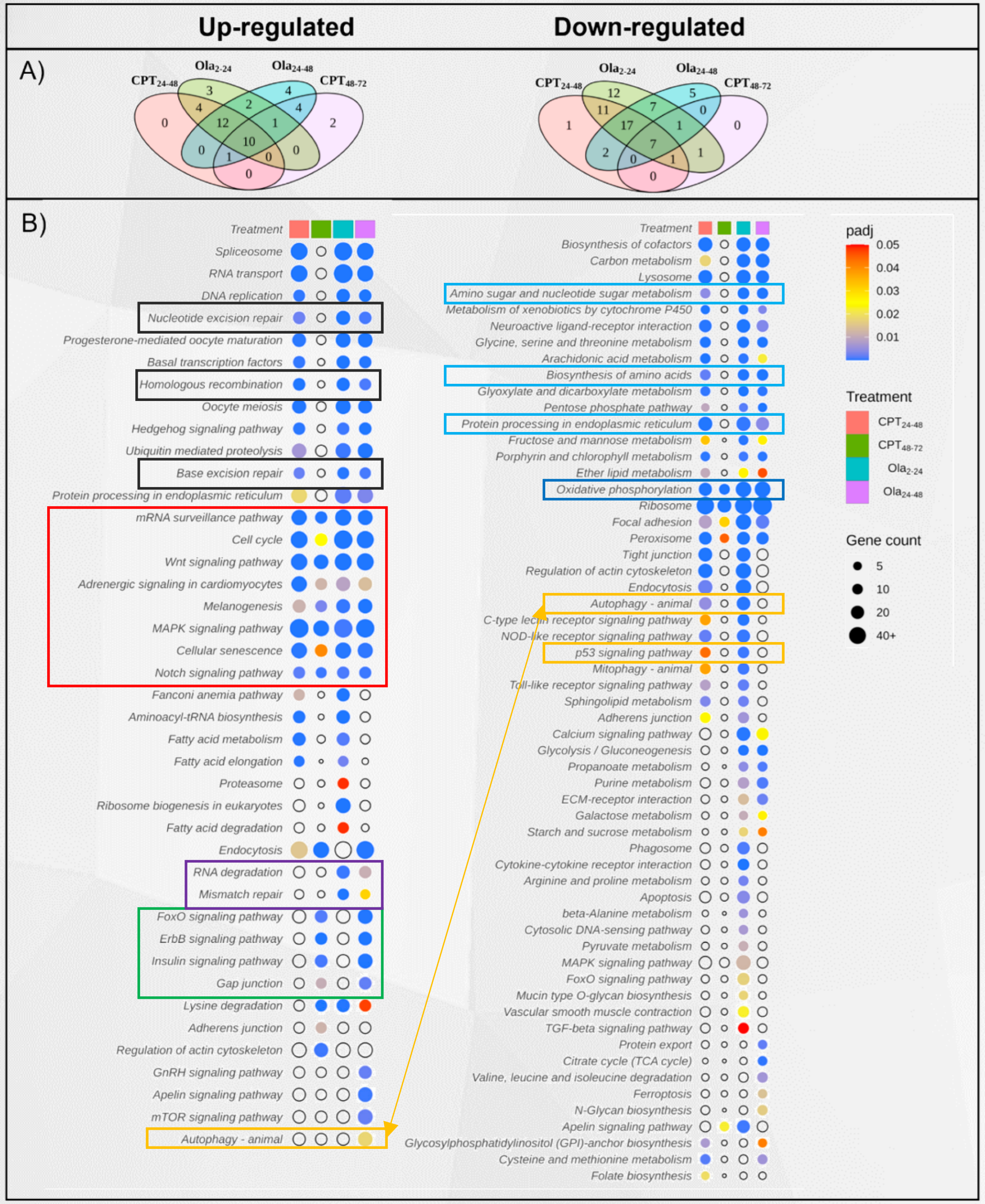
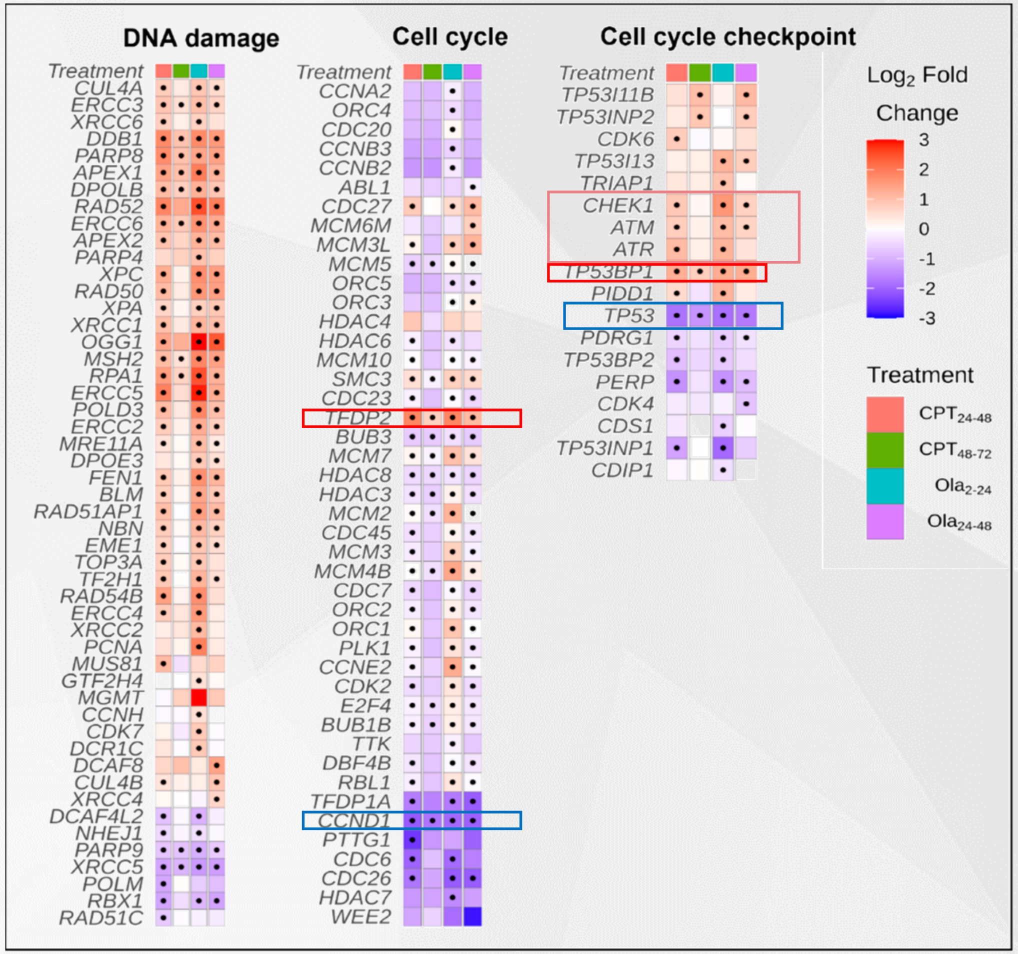
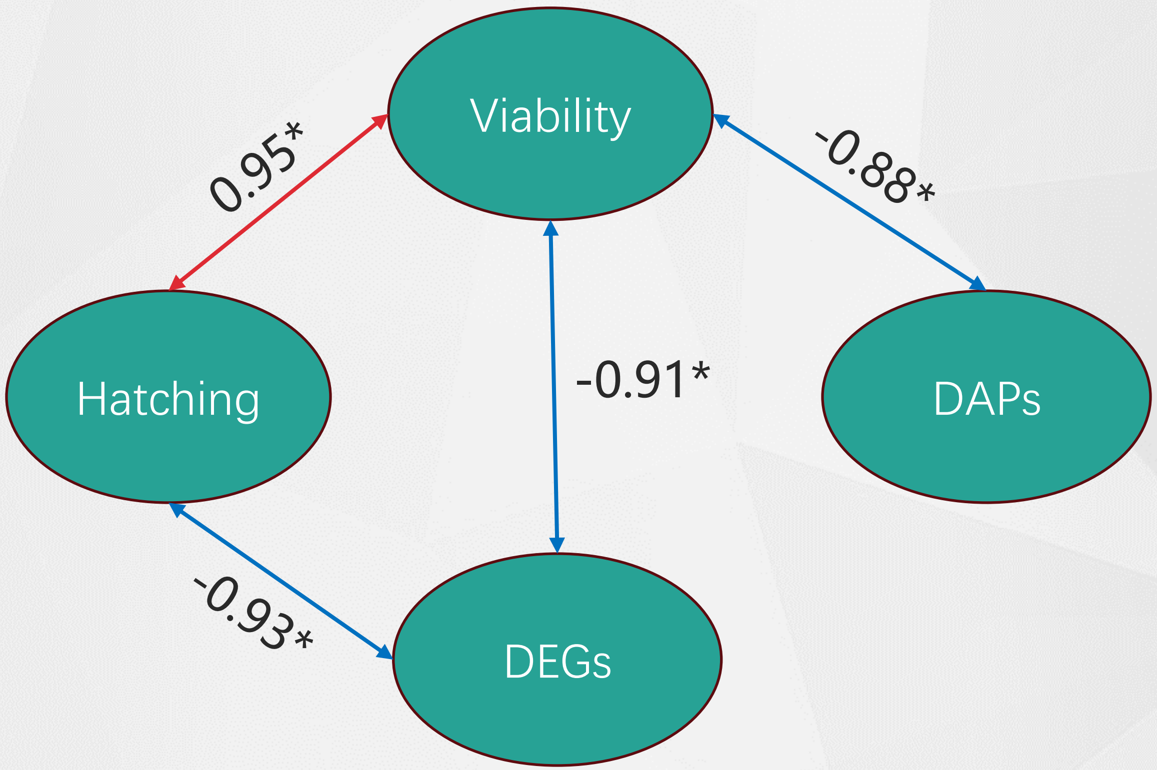


- Upregulated genes in DNA repair, cell cycle, and apoptosis pathways.
- Downregulated metabolic pathways.



Result-Correlation



	Viability	Hatching	DNA Fragmentation	DEGs	DAPs
Viability	1.00	**0.95 ***	−0.73	**−0.91 ***	**−0.88 ***
Hatching	**0.95 ***	1.00	−0.62	**−0.93 ***	−0.87
DNA fragmentation	−0.73	-0.62	1.00	0.73	0.38
DEGs	**−0.91 ***	**−0.93 ***	0.73	1.00	0.68
DAPs	**−0.88 ***	−0.87	0.38	0.68	1.00

Conclusion & Discussion

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Early-stage exposure → ↑ DNA damage ↑ DDR ↓ Metabolism ↓ Viability ↑ Malformation

Late-stage exposure → Slight effects

Implications for Sturgeon Aquaculture:

- DNA damage at early stages could significantly impact embryo survival, hatching, and development.
- Understanding DDR in sturgeons may aid in improving the resilience of these species in aquaculture.

Future Directions

Long-term effects of genotoxicant exposure on sturgeon development.

The role of proteins in stress response.

Additional biomarkers for toxicological studies in aquatic organisms.

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Thanks for listening!