





photo: cc-by via flickr: jordansorensen

1. **Introduction**
The purpose of this study is to investigate the effects of a new drug on the treatment of a specific condition. The study was conducted over a period of 12 weeks, involving 100 participants who were randomly assigned to either the treatment group or the control group. The primary outcome was the reduction in the number of symptoms experienced by the participants in the treatment group compared to the control group. The results of the study are presented in the following sections.

1

2. **Methods**
The study was a randomized, double-blind, placebo-controlled trial. The participants were recruited from a local hospital and were screened for any conditions that might affect the results of the study. The treatment group received the new drug, while the control group received a placebo. The participants were followed up for 12 weeks, and their symptoms were recorded at regular intervals. The data were analyzed using statistical methods to determine the significance of the results.

2

3. **Results**
The results of the study showed that the treatment group had a significantly greater reduction in the number of symptoms compared to the control group. The mean number of symptoms in the treatment group was 15, while the mean number of symptoms in the control group was 25. The difference between the two groups was statistically significant (p < 0.05). The results suggest that the new drug is effective in reducing the number of symptoms in the treatment of the condition.

3

4. **Discussion**
The findings of this study support the use of the new drug in the treatment of the condition. The reduction in the number of symptoms in the treatment group compared to the control group is a clear indication of the drug's effectiveness. However, it is important to note that the study was limited to a 12-week period, and the long-term effects of the drug are not yet known. Further research is needed to confirm the results of this study and to determine the optimal dosage and duration of treatment.

4

5. **Conclusion**
In conclusion, the study has shown that the new drug is effective in reducing the number of symptoms in the treatment of the condition. The results are promising and suggest that the drug may be a valuable addition to the current treatment options. Further research is needed to confirm the results and to determine the optimal treatment regimen.

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1. Smith, J. (2018). The effects of a new drug on the treatment of a specific condition. *Journal of Medical Research*, 15(2), 123-135.
2. Jones, A. (2019). A randomized, double-blind, placebo-controlled trial of a new drug in the treatment of a specific condition. *Medical Journal*, 148(1), 45-55.
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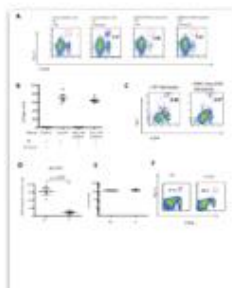
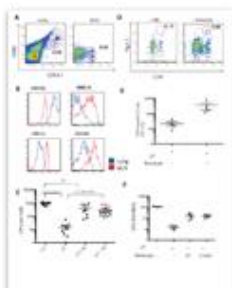
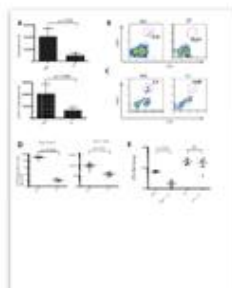
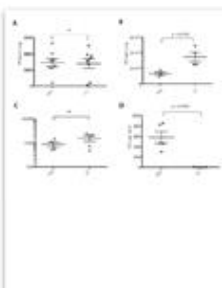
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Ivan Grubisic



Michael Aufreiter



Graham Nott

Concept, prototype testing, development

front end, javascript, interface, development

xml workflows and back end, image processing

A DNA Repair Complex Functions as an Oct4/Sox2 Coactivator in Embryonic Stem Cells

Yick W. Fong, Carla Inouye, Teppei Yamaguchi, Claudia Cattoglio, Ivan Grubisic, Robert Tjian

Text-centric Figure-centric

unambiguously and systematically test and identify transcriptional cofactors that may be directly required to potentiate Oct4- and Sox2-dependent gene activation of *Nanog*. Here, we report the biochemical purification and identification of a multisubunit stem cell coactivator (SCC) that is required for the synergistic activation of *Nanog* by Oct4 and Sox2 in vitro. After extensive biochemical characterization, we surprisingly found that SCC is none other than the XPC-RAD23B-CETN2 (XPC) nucleotide excision repair (NER) complex. SCC/XPC interacts directly with Oct4 and Sox2 and co-occupies a majority of Oct4 and Sox2 targets genome-wide in mouse ES cells. Importantly, SCC/XPC is required for stem cell self-renewal and efficient somatic cell reprogramming. Thus, our findings unmask an unanticipated selective coactivator role of an NER complex in transcription in the context of ES cells and may provide a previously unknown molecular link that couples stem cell-specific transcription to DNA damage response with potential implications for enhanced ES cell genome stability.

Results

Detection of an Oct4- and Sox2-Dependent Coactivator Activity in EC and ES Cells

Having chosen the *Nanog* promoter as our model template, we next set out to develop an in vitro reconstituted transcription assay that could recapitulate the Oct4- and Sox2-dependent transactivation at the *Nanog* promoter observed in vivo. To enhance the sensitivity of the assay, we inserted four copies of the *Nanog* oct-sox-binding sites immediately upstream of the native oct-sox element found in the human *Nanog* promoter. Our basal in vitro transcription assay consisted of purified recombinant TFIIA, -B, -E and -F together with immunopurified native RNA polymerase II, TFIID, and TFIIF (Figure S1A available online). When purified Oct4 and Sox2 were added to this reconstituted transcription system, only a very weak activation of the *Nanog* promoter was detected (Figure 1A, lanes 1 and 2). As a control, we could show that the same complement of general transcription factors (GTFs) was able to support strong Sp1-dependent activation from a GC box-containing "generic" transcription template (G3BCAT) (Figure 1A, lanes 5 and 6). This initial result suggested that efficient activation of *Nanog* by Oct4 and Sox2 may require additional cofactors to potentiate a full activator-dependent response.

We reasoned that such a putative coactivator ought to be selectively active in pluripotent cell types that express *Nanog* under the control of Oct4 and Sox2. For example, NTERA-2 (NT2) is a pluripotent human embryonal carcinoma (EC) cell line that expresses Oct4, Sox2, and *Nanog* and shares with ES cells core molecular mechanisms that govern self-renewal (Pal and Ravindran, 2006). Detailed expression profiling of NT2 and bona fide human ES cell lines revealed many similarities, including robust expression of *Nanog* (Schwartz et al., 2005 and Sperger et al., 2003). However, unlike human ES cells, NT2 cell culture can be more readily scaled up, a prerequisite to generating sufficient quantities of starting materials for the biochemical purification of putative Oct4/Sox2 coactivators. We therefore chose extracts derived from NT2 cells as our starting materi-

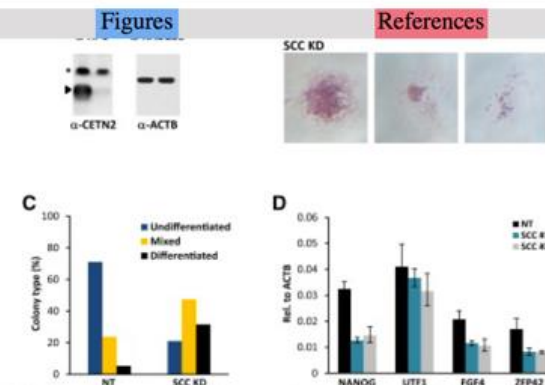
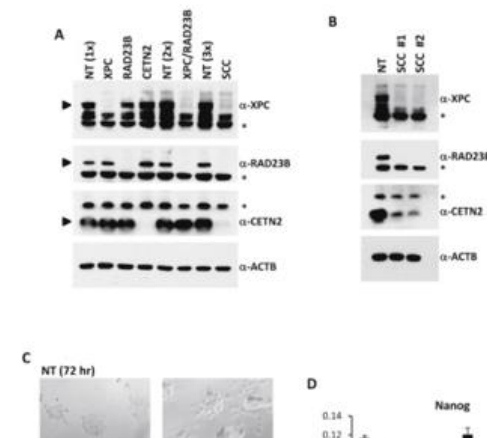


Figure 5. SCC Is Required for ES Cell Maintenance (A) Efficiency of shRNA-mediated depletion of SCC in ES cells. Whole-cell extracts of mouse D3 cells infected with nontarget (NT) lentiviruses (MOI of 300) or with an equal mixture of three lentiviruses (MOI of 100 each) targeting XPC, RAD23B, and CETN2 (SCC KD) are analyzed by western blotting. XPC, RAD23B, and CETN2 levels are indicated by filled arrowheads. Asterisks denote nonspecific signals. (B) ES cell morphology and alkaline phosphatase (AP) activity (red) are maintained in control D3 cells (NT, top) but are significantly reduced in SCC-depleted D3 cells (SCC KD, bottom). See also Figure S4C. (C) Clonal assays on SCC-depleted D3 ES cells. Differentiation status was scored based on AP staining intensity, ES cell morphology, and colony morphology. Nonoverlapping sets of shRNAs targeting SCC (SCC #1 and SCC #2) are used to deplete SCC. Quantification of *Zfp42* mRNA levels are analyzed by real-time quantitative PCR (qPCR) and normalized to *Actb*. Data from three independent experiments are shown; error bars represent standard deviations. n = 3. See also Figure S4.



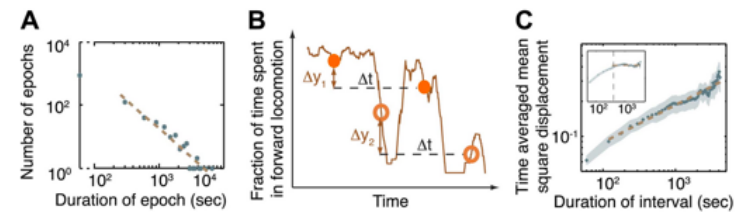
A longitudinal study of *Caenorhabditis elegans* larvae reveals a novel locomotion switch, regulated by Gas signaling

Stanislav Nagy Charles Wright Nora Tramm
Nicholas Labello Stanislav Burov David Biron

Abstract

Despite their simplicity, longitudinal studies of invertebrate models are rare. We thus sought to characterize behavioral trends of *Caenorhabditis elegans*, from the mid fourth larval stage through the mid young adult stage. We found that, outside of lethargus, animals exhibited abrupt switching between two distinct behavioral states: active wakefulness and quiet wakefulness. The durations of epochs of active wakefulness exhibited non-Poisson statistics. Increased G_{as} signaling stabilized the active wakefulness state before, during and after lethargus. In contrast, decreased G_{as} signaling, decreased neuropeptide release, or decreased CREB activity destabilized active wakefulness outside of, but not during, lethargus. Taken together, our findings support a model in which protein kinase A

Figure 3.



The dynamics of the active wakefulness state during the three hours prior to L4 lethargus in wild-type animals.

(A) A histogram of the durations of epochs of active wakefulness plotted on a log-log scale. Epoch durations longer than 3 min exhibited a power-law distribution with an exponent $-(1+\alpha) = -1.83 \pm 0.31$. (B) Two displacements along the y-axis of a sample trace of the fraction of forward locomotion, Δy_1 (between filled circles) and Δy_2 (between empty circles). Both displacements correspond to an identical time interval, Δt . The time-averaged mean square displacement (TMSD) is calculated in two steps: (i) using a sliding window to calculate the mean squared displacements along traces of each of the individual animals (Golding and Cox, 2006); (ii) averaging the results obtained from the previous step for all animals. (C) The TMSD plotted on a log-log scale as a function of the time-interval, Δt . The TMSD was calculated for the subset of $N = 20$ animals where data 3 hr prior to the onset of L4leth was available ($N = 20$). The TMSD exhibited power-law growth with the exponent $(1-\alpha) = 0.32 \pm 0.03$, consistent with a value of $\alpha \approx 0.7$. Inset: for the purpose of illustration, the TMSD for a two-state Markov chain with a comparable mean duration of epochs is shown to reach its saturation value at $\Delta t \approx 400$ s (vertical dashed line).

DOI: <http://dx.doi.org/10.7554/eLife.00782.005>

Figure 4.

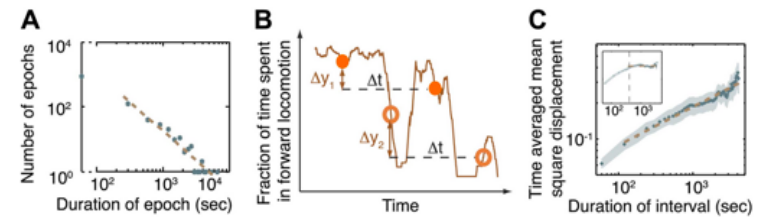
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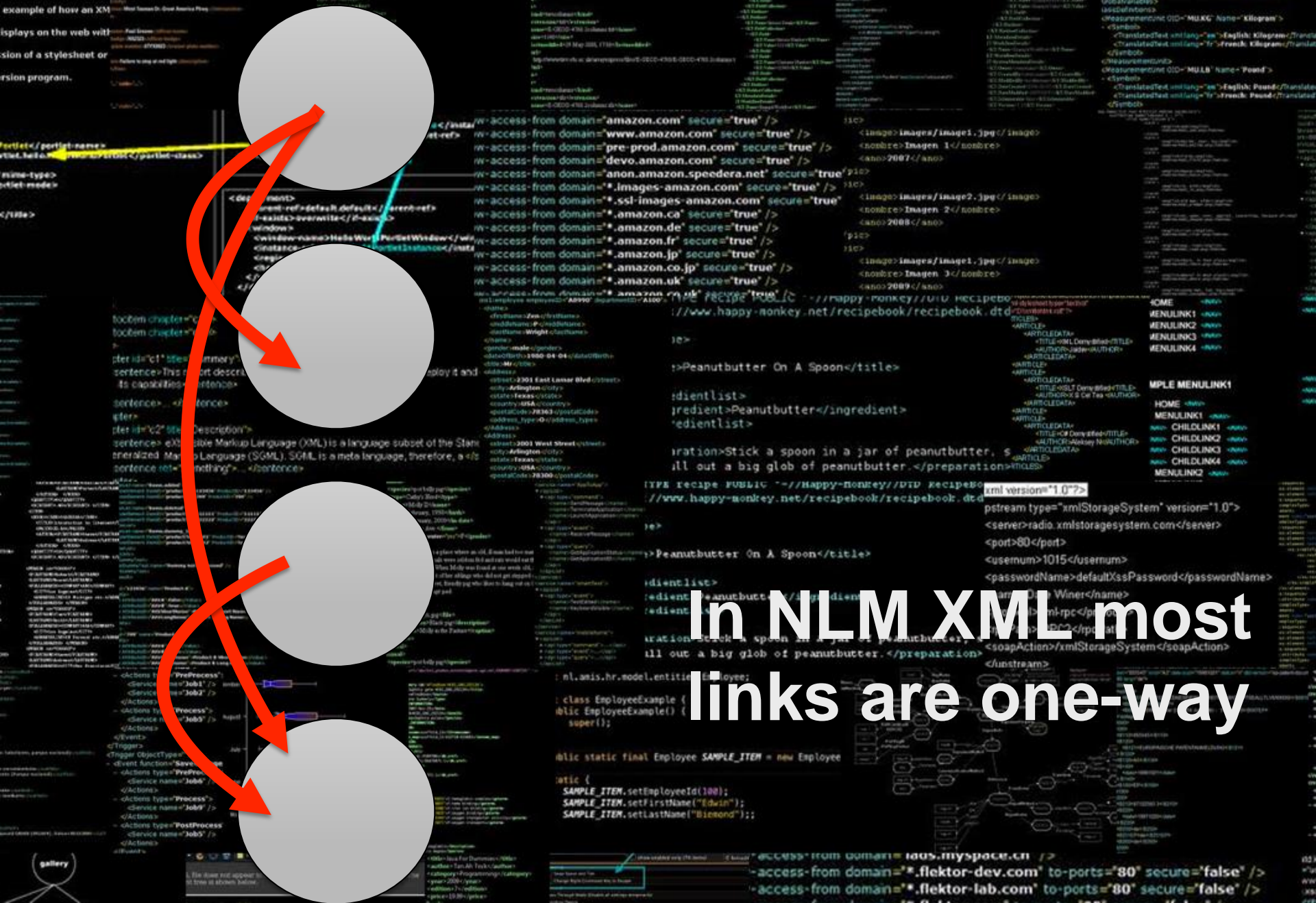


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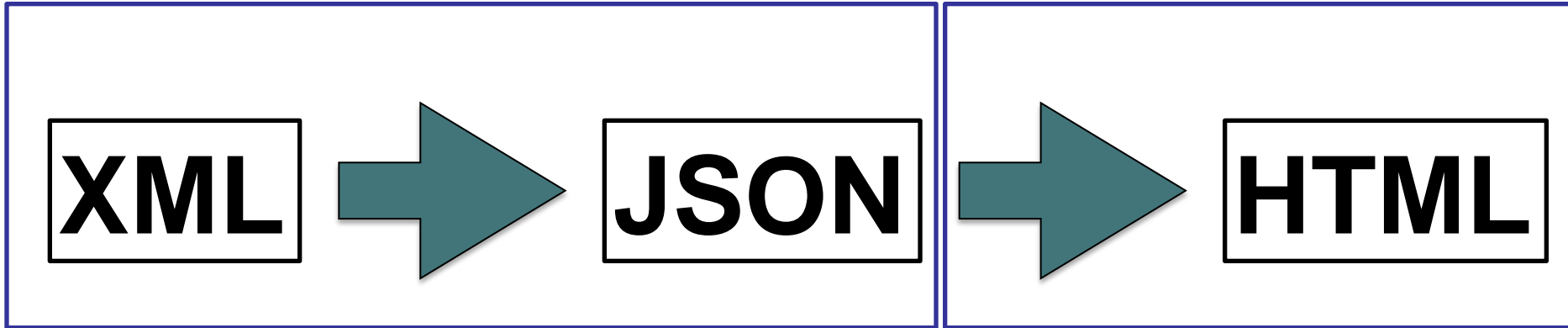


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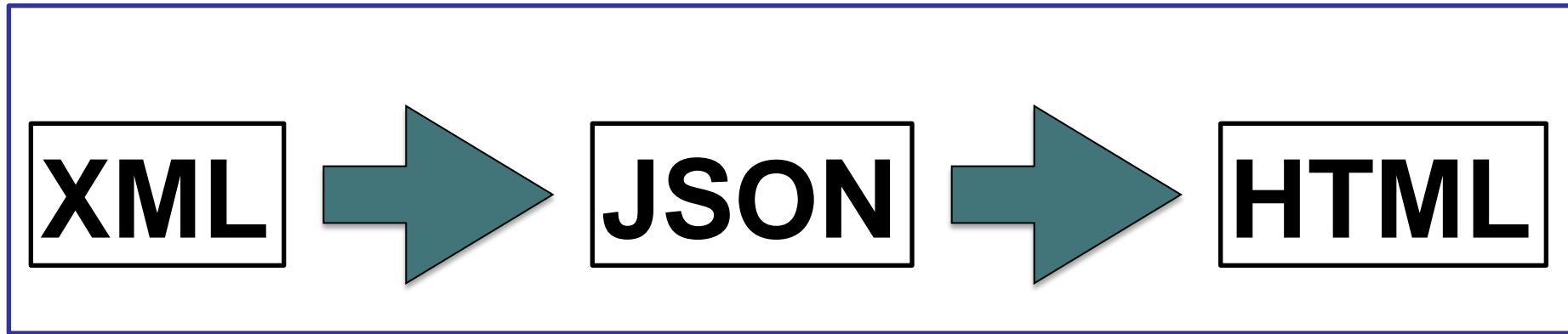
**In Lens JSON we
make two-way links
explicit**

Lens V0.1



Server using node.js

Browser javascript



Put ALL THE THINGS IN THE Browser javascript

Quantification of gait parameters in freely walking wild type and sensory deprived *Drosophila melanogaster*

César S Mendes Imre Bartos Turgay Akay Szabolcs Márka Richard S Mann

Abstract

Coordinated walking in vertebrates and multi-legged invertebrates such as *Drosophila melanogaster* requires a complex neural network coupled to sensory feedback. An understanding of this network will benefit from systems such as *Drosophila* that have the ability to genetically manipulate neural activities. However, the fly's small size makes it challenging to analyze walking in this system. In order to overcome this limitation, we developed an

Contents Figures References Article Info

Abstract Main Text

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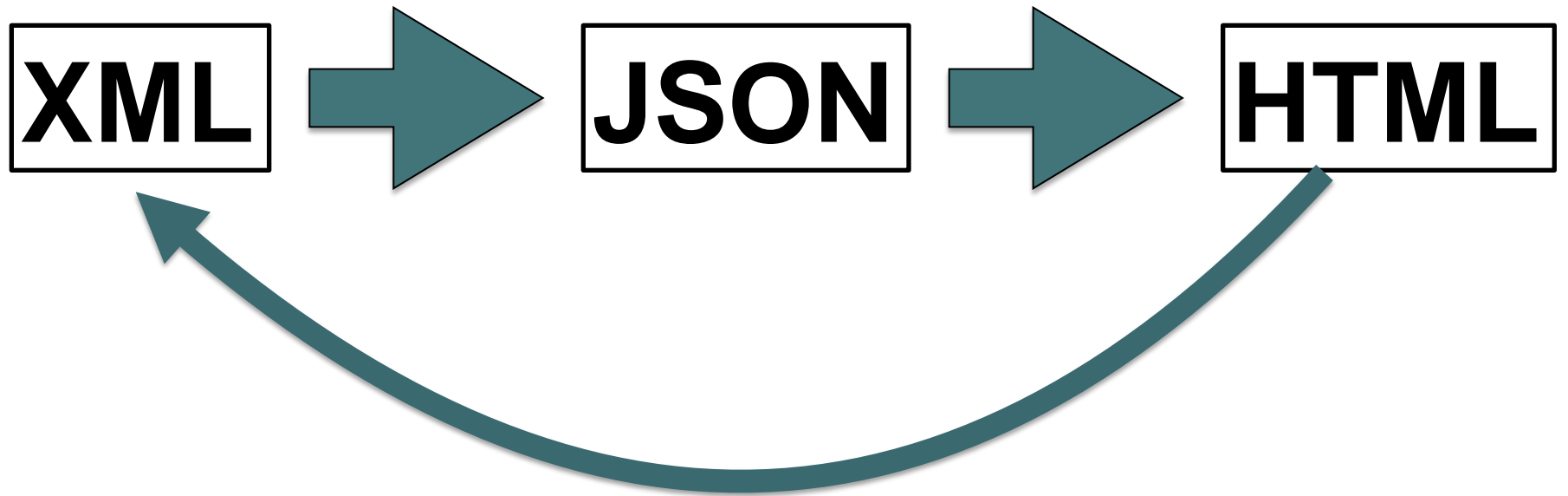
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1 - Call the Javascript

2 - Point at an XML file

Lens V0.??



edit in browser

NOW

The screenshot shows the eLife website interface for a research article. At the top, the breadcrumb navigation reads 'eLife > Research article > Biophysics and structural biology / Cell biology'. Below this are tabs for 'Article', 'Figures & data', 'Metrics', and 'Article & author info'. The main title is 'Massive endocytosis triggered by surface membrane palmitoylation under mitochondrial control in BHK fibroblasts'. The authors listed are Donald W Hilgemann, Michael Fine, Maurine E Linder, Benjamin C Jennings, and Mei-Jung Lin. The article is published by the University of Texas Southwestern Medical Center and Cornell University College of Veterinary Medicine. The DOI is <http://dx.doi.org/10.7554/eLife.01293>, published on November 26, 2013. The citation is 'eLife 2013;2:e01293'. The abstract begins with 'Large Ca transients cause massive endocytosis (MEND) in BHK fibroblasts by nonclassical mechanisms...'. On the right side, there is a red button 'View article with eLife Lens' and a 'Reference tools' section with 'DOWNLOAD' and 'OPEN SHARE' options. A 'Jump to:' section lists various article components like 'Abstract', 'eLife digest', 'Main text', etc. A blue arrow points from the word 'NOW' to the 'View article with eLife Lens' button. Another blue arrow points from the 'View article with eLife Lens' button to the abstract text.

NEXT



Peer Review

submissions system

EJP



typesetters

TNQ



80% XML

80% XML + lens.js

=

Awesome reviewing experience

proteins were found to be involved in the multiple cellular process like transcription, telomerase core complex assembly, cell cycle progression, apoptosis, snoRNPs biogenesis, PIKK mediated signaling, RNA polymerase II assembly, as well as in the mitosis.⁵⁻⁷ Recently human RuvB1 and RuvB2 are in the focus because of their involvement in many human cancers⁸ like hepatocellular carcinomas,⁹ renal and gastric carcinomas.¹⁰ The biochemical characterization reports on RuvB like proteins established that these are active ATPase and many reports have also shown their helicase activity.⁶ Due to the presence of ATPase activity and involvement in multiple cellular processes these proteins have been categorized as AAA+ proteins (ATPases associated with multiple cellular processes).

Pih1 is an unstable protein however stabilizes itself after interaction with Hsp90 and Tah1.² Pih1 interacts with snoRNPs factor Nop1/fibrillarin, Nop58, Tel2, Monad and play crucial role in snoRNPs biogenesis and PIKK signaling.¹¹ Tah1 is characterized as the cofactor of Hsp90 and enhances the activity of Hsp90 protein.¹ Human counterpart of Tah1 is known as RPAP3 which is almost 6 times bigger in terms of number of amino acid as well as in number of TPR repeat. Yeast Tah1 contains 2 TPR repeats while RPAP3 contains 6 TPR repeats.

R2TP complex has been found to play an important role in many processes like RNA polymerase-II assembly, snoRNPs assembly, PIKK signaling, and in the apoptosis.¹¹ R2TP-Hsp90 complex together with Perfoldin like complex interacts with RNA polymerase-II and was found to be crucial for the assembly of the RNA polymerase-II.⁴ In yeast Pih1 deletion led disruption of R2TP complex resulted into decreased snoRNAs of box C/D.² Human RuvB1 and RuvB2 interact with almost all core box C/D snoRNPs factor and PIH1D1 directly interacts with Nop1, Nop58, and Nop56. RuvBs have been crucial for the box C/D and box H/ACA snoRNA.^{12, 13} The depletion of human RuvBL1 and RuvBL2 showed a decreased level of mature box C/D snoRNA,¹⁴ thus providing the evidence of R2TP complex involvement in snoRNP assembly and biogenesis. Recently it has been discovered that R2TP complexes are also involved in the PIKK (phosphatidylinositol 3 kinase related protein kinase) signaling pathway.¹⁵ RuvB1 and RuvB2

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The screenshot shows a search result for 'R2TP complex'. The top part of the interface has a navigation bar with icons for home, search, and other functions. Below the search bar, there is a text snippet: 'involvement in various activities was prepared on the basis of reported role in yeast and human. R2TP complex is involved in the diverse cellular activities shown in the figure.' Below this, there is a green button labeled 'Image' with a camera icon, and a note that says 'mentioned 2 times'. The main content area shows two sections, 'A Motifs of LdRuvB1' and 'B Motifs of LdRuvB2'. Each section contains a horizontal bar chart with various colored segments representing different motifs. The legend for section A includes: 'AAA + ATPase domain', 'TPK C terminal', 'Nucleic acid binding, OB-fold like', and 'Helicase'. The legend for section B includes: 'AAA + ATPase domain', 'TPK C terminal', 'Nucleic acid binding, OB-fold like', and 'Helicase and TPR'. The bottom part of the screenshot shows a caption: 'Figure 2. In-silico prediction of conserved motifs of RuvB from *L. donovani* using InterProScan. (A) Predicted motifs model of *L. donovani* RuvB1 was prepared, which

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Landes Biosciences, PeerJ also interested are PLOS, Dove Press and a project from the University of California Davis

Contributors

Commits

Code Frequency

Punchcard

Use ← and → to navigate



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Time's Up!

About your speaker:

Name: Ian Mulvany

Company: eLife

Tel:

Email: i.mulvany@elifesciences.org

Social Media: [@IanMulvany](#)

