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Editorial office
World Journal of Stem Cells

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Ihre Nachricht vom:
Unser Zeichen:

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Datum: 29.07.2020

Dear Editor on board,

We thank you and the reviewers, for the opportunity to revise our manuscript entitled "Assessment of Tobacco Heating System 2.4 on osteogenic differentiation of mesenchymal stem cells and primary human osteoblasts compared to conventional cigarettes" [Manuscript NO: 54923].

We appreciated the reviewers' comments. We have addressed all issues raised by the reviewers and edited the manuscript accordingly. The detailed answers to the questions raised by the reviewers are summarized below. All changes performed in the manuscript are highlighted.

We would like to resubmit our revised manuscript to *World Journal of Stem Cells* and hope that the revised manuscript meets now the high standards of this journal.

All authors have approved the final submitted manuscript and no conflict of interest exists between the authors.

We are looking forward to your final decision of the manuscript

Yours sincerely,

Prof. Andreas Nüssler

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

We would like to thank the reviewer for his/her careful reading and insightful comments on the manuscript. We have taken the comments on board to improve and clarify the manuscript. Please find below a detailed point-by-point response to all comments (printed in blue)

Specific Comments to Authors: The manuscript by Aspera-Werz and colleagues is an interesting study on the effects of tobacco heating system (THS) 2.4 and conventional cigarette smoking (CS) on the viability and osteogenic differentiation abilities of human immortalized mesenchymal stem cells and primary human osteoblasts, with the aim of elucidating possible advantages of THS over CS on bone healing in smokers. The text is clearly written; there are only a few typos that may be easily corrected, as for example: - Fig. 1A.: min/stick, instead of min/stuck on the vertical axis - Various sections in Materials and Methods, where the authors indicate that measurements were “correct to the background”, instead of saying “corrected” - Last line in section “THS is less toxic to bone cells than conventional.....”: it should state that “MSCs were more sensitive to AE....”, not “sensible”

We would like to thank the reviewer for his/her comment. We have corrected the typos in the manuscript, as the reviewer suggested. Additionally, the manuscript was edited by a Professional English Proofreading Service.

As main comments to the manuscript, I have lacked, as a reader who is not familiar with the generation of aqueous extracts (AEs) from cigarettes, a series of explanations in the text, a discussion on a number of points that may clarify the experimental set up and the ultimate significance of the obtained data to those who may not be wholly familiar with the approach that has been followed:

- Does the system employed (gas washing bottle, peristaltic pump) take into account the fact that the cigarette will be burned while the THS will not?

We would like to thank the reviewer for his/her observation. The system employed to generate the aqueous extracts from cigarettes and Tobacco heating system (THS) sticks are implemented in several laboratories and resemble the principle of the smoking machines used to produce aqueous extract on a large scale. The fact that the cigarette is combusted and THS only heated does not make any difference or influence in the production of the extracts. But it should be considered that the extracts have to be prepared with the puff regimen to avoid the improper operation of THS device (which could happen with a continuous regimen where the peristaltic pump generates a constant negative pressure). Noteworthy, it is not possible to overheat the THS stick due to the fact that the device only heats the stick a certain number of times, and for a certain time. In case of exceeding one or the other, the device turns off automatically. Additionally, the puff regimen, under the standard of Health Canada smoking regime, represents better the human smoking behavior than the continuous regimen.

- Does the system mimic the entry of the molecular species in blood? In other words, would the addition of AEs to the medium reflect the species that cross into the blood stream? Otherwise, should the model not include other elements such as endothelial cells, to investigate the crossing of the putative toxic molecules through some kind of “biological barrier”? Considering the crossing into the



blood stream, could the differences in the concentration of particles in the AEs give rise to differences in the molecular species that cross from THS and from CS.

We would like to thank the reviewer for highlighting this point. The aqueous extracts were generated with identical volumes (medium) and amount of puffs - representing the smoking behavior. The medium was sterile filtered before application to the cells, such that particles with a size $> 0.2 \mu\text{m}$ were removed – comparable to the barrier function in the lung. However, we agree with the reviewer that the addition of endothelial cells or immune cells would improve the model to represent better the molecular species that cross into the bloodstream. However, this would also increase the complexity of the model system and may interfere with cell specific analysis. Its application to multiple interconnected cell culture systems, representing functionalities of different organs, could allow investigating the cross-talk between different organs through circulating medium. However, this highly complex system was not applied in this study.

- The study indicates a reduced effect of THS on MSC and hOB viability and differentiation abilities in support of a less harmful action of THS on bone regeneration following fracture. However, the authors have not taken into account the conditions present following damage to the tissue when establishing the culture system, e.g. presence of cytokines in the medium. These might alter the action of the various toxins that are present in the AEs. It would be highly desirable for the authors to discuss these points in the manuscript, preferably supporting the arguments with available evidence and published data that support the validity of their model.

We would like to thank the reviewer for his/her suggestion and modified the discussion section. The aim of this exploratory study was to elucidate the effect of THS on bone-forming cells viability and function. Our study demonstrated that THS has less impact on the viability and function of bone-forming cells. These results suggest that appropriated bone homeostasis is not negatively affected by THS. However, our study cannot demonstrate the beneficial effect of THS during fracture healing. Following, fracture levels of TGF- β 1 increase to attract MSCs to the fracture place. Interestingly, smokers and patients with delayed fracture healing have lower TGF- β 1 blood levels compared to non-smokers. Until now, it is not known if the levels of TGF- β 1 are affected by THS. Therefore, additional experiments in co-culture system that represent the remodeling process of the bone are need to elucidate the role of THS on delayed fracture healing.

As a minor point: The authors indicate in section “THS has less effect on cell viability....”, lines 12-13, that Figure 2C shows calcein-AM staining of SCP-1 cells, while the legend in this Figure indicates that the staining corresponds to hOBs.

We would like to thank the reviewer for his/her observation and apologize for the mistake. We have changed the figure legend accordingly



Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

We would like to thank the reviewer for his/her careful reading and insightful comments on the manuscript. We have taken the comments on board to improve and clarify the manuscript. Please find below a detailed point-by-point response to all comments (printed in blue)

Specific Comments to Authors: There are minor linguistic errors in the manuscript.

We would like to thank the reviewer for his/her observation. We have corrected several linguistic mistakes in the manuscript. Additionally, the manuscript was edited by a Professional English Proofreading Service.



Reviewer #3:

Scientific Quality: Grade E (Do not publish)

Language Quality: Grade D (Rejection)

Conclusion: Rejection

We would like to thank the reviewer for his/her careful reading and insightful comments on the manuscript. We have taken the comments on board to improve and clarify the manuscript. Please find below a detailed point-by-point response to all comments (printed in blue)

Specific Comments to Authors: Thank you very much for submitting your research to the World Journal of Stem Cells. The reviewer would like to make several comments on your article.

1.What is the novelty of this report?

We would like to thank the reviewer for his/her suggestion. This study is the first that evaluates the effect of Tobacco heating system (THS) on bone-forming cells function and differentiation. The novelty of this study is that THS showed less detrimental effects than conventional cigarettes on MSCs under osteogenesis and primary human osteoblast. Moreover, THS did not induce oxidative stress in the cells and does not affect primary cilia structure (organelle that coordinates signaling pathways involved in osteogenic lineage) Our results, demonstrated that THS could be a potentially less harmful alternative for maintaining the bone homeostasis in smoker which don't want or fail to quit smoking.

2.How did the authors calculate the sample size? How did the authors arrive at the number of participants.

We would like to thank the reviewer for his/her observation. The sample size applied in this study was the minimum required for *in vitro* studies. The experiments that involved cell lines (SCP-1 cells) were performed with 3 biological replicates (N) and between 2 and 3 technical replicates. The experiments that involved primary human osteoblast, were performed with 5 biological replicates (N) and between 2 and 3 technical replicates. The biological replicates were handled independently on different days (including cell isolation, treatment, and variables measure) to avoid pseudoreplicates that could lead to spurious statistical significance. All statistical methods of this study were reviewed by the Institute for Clinical Epidemiology and Applied Biometry at the University of Tübingen.

3.Please comment on the individual differences.

We would like to thank the reviewer for his/her comment. In this exploratory study there weren't any variable measure directly in the participants that could be influenced by individual differences between the participants. However, since the primary human osteoblast were isolated from different donor's bone sample, we should consider that this culture represents the natural donor differences which is not represented in cell lines cultures (*e.g.*, SCP-1 cells). Additionally, primary human osteoblast are no cancerous or genetically transformed cells. Therefore, primary human osteoblasts are so-called "golden standard" for cell culture experiment in bone forming cells.



4. Did the participants agree for the publication?

We would like to thank the reviewer for his/her observation. As reported in the material and methods section, prior to inclusion, all participants (donors of the bone samples for human osteoblast isolation) gave their written informed consent.

Additionally, we would like to declare that the study was conducted following the 1964 Declaration of Helsinki (Ethical Principles for Medical Research Involving Human Subjects) and was approved by the local ethics committee from the University Hospital of Tübingen.

5. Please perform additional experiments to elucidate the underlying mechanism.

We would like to thank the reviewer for his/her comment. As reported in the manuscript, our previous studies have demonstrated that oxidative stress induced by compounds produced during conventional cigarette combustion may be one of the factors responsible for the impaired osteogenic differentiation of bone-forming cells and osteogenic precursor cells. Additionally, the detrimental effect of cigarette smoking on primary cilia structure due to oxidative stress; impairs signaling pathways involved in the appropriate osteogenic differentiation of MSCs. Since nicotine and cotinine were not directly involved in the impaired osteogenic differentiation observed under cigarette smoke exposure, we were interested in performing this exploratory study to compare THS (electronic nicotine delivery system) with conventional cigarettes. This study aimed to elucidate if THS showed the same levels of toxicity than conventional cigarettes on bone-forming cells. Moreover, ROS levels and primary cilia structure were detected to elucidate if the same mechanism in impaired osteoblast function were involved in THS. For the reason that THS did not increase oxidative stress levels and maintained primary cilia structure, we can conclude that the mechanisms involved in cigarette smoke impair osteogenic differentiation on MSCs are not taking place under THS treatment. However, in future, we are interested in elucidating the role of THS on bone homeostasis thought to regulate bone-resorbing cells (osteoclast) and if this regulation influences bone-forming cells (osteoblast).

6. Please comment of the clinical relevance. Thank you very much.

We would like to thank the reviewer for highlighting this point. Since 1976, several studies confirmed the positive correlation between the number of cigarettes consumed and reduced bone mass [1-3]. Additionally, it was demonstrated that cigarette consumption imbalances bone homeostasis, causing secondary osteoporosis, osteoarthritis, and fragility fractures [4-7]. Furthermore, cigarette consumption is associated with increased risk of delayed fracture healing [8], non-union [9, 10], or complications (e.g., infections, implants revision) [11-13], leading to extended hospital stays [9, 12, 14-16].

Consequently, cigarette consumption caused an increase in the health system cost; for example, in Germany, the costs associated with cigarette consumption in the health system are around 80 billion euros per year [17]. Therefore, the development of alternatives that maintain bone homeostasis or protect the bone structure in smokers are strongly needed. So, the clinical relevance of our study is that THS could be a potentially promising alternative for smokers to maintain appropriate bone homeostasis and delay development of secondary osteoporosis. We have adapted the discussion according to the reviewer's suggestion.



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Reviewer #4:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

We would like to thank the reviewer for his/her careful reading and insightful comments on the manuscript. We have taken the comments on board to improve and clarify the manuscript. Please find below a detailed point-by-point response to all comments (printed in blue)

Specific Comments to Authors: Study is well designed and experimental replicates are acceptable. Introduction and discussion are adequate. Figure 1A y-axis 'min/stuck' needs to be rectified to min/stick. Work may be inetersted to those in concerned field.

We would like to thank the reviewer for his/her comment and apology for the mistake. We have changed the label of the y-axis in Figure 1A accordingly.





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Datum: 09.06.2020

Dear Prof. Ya-Juan Ma,

We like to thank you and the reviewer, for the opportunity to revise our already revised manuscript entitled "Assessment of Tobacco Heating System 2.4 on osteogenic differentiation of mesenchymal stem cells and primary human osteoblasts compared to conventional cigarettes" [Manuscript NO: 54923].

We appreciated the reviewer comments and have addressed all issues raised by this reviewer and edited the manuscript accordingly. The detailed answers to the questions are summarized below. All changes performed in the manuscript are highlighted. However, I am a little bit puzzled by the request of all raw data. Does this mean that you have a doubt in our data or is this a new routine request? Of course, we have done so for transparency; but it is a bit unusual for me who is asked at the same time being part of the editorial board and has been invited for this paper. But as already pointed out we have done so as requested including the certificate of statistics from the Institute for Clinical Epidemiology and Applied Biometry at the University of Tübingen.

We trust you for a fair judgement of our resubmitted revised manuscript to *World Journal of Stem Cells* and are convinced that the new changes will now meet the high standards of this journal.

All authors have approved the final submitted manuscript and no conflict of interest exists between the authors or other third parties regarding the content of the manuscript.

We are looking forward to your final decision of the manuscript.

Yours sincerely,

Prof. Andreas Nüssler

Reviewer #1:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: Thank you very much for submitting your revised research to the World Journal of Stem Cells. The reviewer would like to make a couple of comments on your article.

We would like to thank the reviewer for his/her careful reading and insightful comments on the manuscript. We have taken the comments on board to improve and clarify the manuscript. Please find below a detailed point-by-point response to all comments (printed in blue)

1. For Figure 5. It seems that there are background noise in the fluorescent image(s). Please provide images with better quality

We would like to thank the reviewer for his/her suggestion. We have improved the quality of the images in figure 5.

2. Please provide the rationale on selection of posthoc analysis. Please provide the raw data.

We would like to thank the reviewer for his/her comment. We have performed post hoc analysis to explore differences between different groups means. One-way ANOVA test tells whether there is an overall difference between the groups, but it does not tell which specific groups differed as post hoc tests do. All statistical methods of this study were reviewed by the Institute for Clinical Epidemiology and Applied Biometry at the University of Tübingen. Additionally, the raw data for all figures included in the manuscript is provided as requested (please find raw data below "Raw data Manuscript NO 54923")

3. For Figure 6 Please provide the error bars. Please provide the raw data for this. Thank you very much.

We would like to thank the reviewer for his/her observation. We have added the error bars to figure 6. Additionally, the raw data for figure 6 was provided (please find raw data below "Raw data Manuscript NO 54923")



Raw data Manuscript NO 54923

Figure 1

pH		
Cigarette	THS	Medium
6,98	7,95	7,65
7,7	7,75	7,55
7	8,17	8,07
8,08	8,26	8,1
7,97	8,26	8,05
7,69	8,26	8,02
7,49	7,5	7,4
7,43	7,53	7,45
7,61	7,54	7,55
7,64	8,9	7,6
7,85	8,27	8
7,89	8,25	8,1
7,81	8,07	8,5
7,82	8,21	8,6
7,79	8,17	7,9

Time [min]	
Cigarette	THS
3,13	5,19
3,5	5,13
3,5	5,4
3,16	5,48
3,12	5,47
3,15	5,34
3,14	5,49
3,13	5,3
3,13	5,46
3,17	5,13
3,4	5,46
4	5,48
4,2	5,46
3,13	5,32
3,56	5,49
3,05	5,47
3,12	5,22
3,04	5,31
3,03	5,12



OD 320nm		
Cigarette	THS	Medium
0,662	0,257	0,22
0,624	0,253	0,234
0,627	0,265	0,232
0,733	0,254	0,196
0,752	0,243	0,229
0,739	0,256	0,215
0,623	0,243	0,194
0,632	0,244	0,191
0,615	0,273	0,2
0,703	0,244	0,198
0,721	0,23	0,208
0,73	0,24	0,206
0,487	0,243	0,194
0,496	0,245	0,201
0,504	0,24	0,196
0,514	0,241	0,203
0,503	0,243	0,194
0,512	0,23	0,2
0,572	0,258	0,21
0,578	0,255	0,21
0,625	0,259	0,207
0,567	0,258	0,209
0,582	0,258	0,21
0,609	0,271	0,212
0,529	0,264	0,201
0,546	0,276	0,207
0,56	0,272	0,215
0,602	0,254	0,196
0,66	0,253	0,203
0,65	0,266	0,218
0,516	0,252	0,192
0,498	0,247	0,215
0,49	0,24	0,21
0,461	0,243	0,209
0,466	0,237	0,22
0,458	0,232	0,21
0,653	0,251	0,207
0,656	0,248	0,206
0,689	0,246	0,199
0,554	0,261	0,228
0,573	0,262	0,242
0,552	0,256	0,248
0,595	0,262	0,24



OD 320nm		
Cigarette	THS	Medium
0,62	0,264	0,244
0,69	0,257	0,25
0,598	0,258	0,244
0,611	0,246	0,251
0,604	0,235	0,247



Figure 2 Viability 48 hr

hOB N=5 n≥3 (primary cells human donor samples) Resazurin							
	THS [puff/ml]						
crl	4.10 ⁻⁵	4.10 ⁻⁴	4.10 ⁻³	2.10 ⁻²	4.10 ⁻²	2.10 ⁻¹	4.10 ⁻¹
1,003532	1,09509	1,249806	1,277782	1,316779	1,409608	1,172236	0,9848817
0,9916637	1,096786	1,266337	1,383327	1,296856	1,407912	1,24048	0,9115507
1,004804	1,220134	1,277782	1,300247	1,352808	1,426139	1,211657	1,039138
1,038092	1,177639	1,290816	1,246314	1,260599	1,50728	1,026005	0,9117297
1,014468	1,193572	1,218295	1,205659	1,252907	1,317187	1,03095	1,000183
0,9474407	1,121601	1,173794	1,175991	1,188078	1,345206	1,013369	1,017764
1,052542	0,9595117	0,6507495	0,9799104	0,9950548	0,8263019	0,843919	0,6652759
0,9474579	0,9712564	0,7957039	0,8587545	0,9422037	0,9202596	0,7156544	0,5605007
0,9347611	1,028596	1,008047	0,8780639	0,8602377	0,7973508	0,6448379	0,7295123
1,065239	0,9293142	0,9572914	0,971899	1,043204	0,8847487	0,6755385	0,885739
1,153486	0,9919995	0,8782694	0,9422734	0,8723614	0,8812234	0,7709398	0,3598375
1,064866	0,89944	0,7167826	0,7236753	0,6818266	1,123454	0,657702	0,2141055
0,9521201	0,7763554	0,6064988	0,8955013	0,6252077	0,7507539	0,5690812	0,2869715
0,829528	0,8482368	0,5720352	0,8930396	0,6567174	0,8393747	0,6586867	0,5420026
1,047294	1,032009	0,7545584	0,7957607	0,7080397	0,7269795	0,5970594	0,5598444
0,9336554	0,8206815	0,6246383	0,7412674	0,6542109	0,5940689	0,538911	0,482424
1,01905	0,7359509	0,6708248	0,5708095	0,7100334	0,5279458	0,3794183	0,3890543

hOB N=5 n≥3 (primary cells human donor samples) Resazurin							
	Cigarette [puff/ml]						
crl	4.10 ⁻⁵	4.10 ⁻⁴	4.10 ⁻³	2.10 ⁻²	4.10 ⁻²	2.10 ⁻¹	4.10 ⁻¹
1,034161	0,9771769	1,009865	1,103072	0,9851282	0,6869559	0	0,01021516
0,9621579	0,9740848	1,081427	1,137527	1,024884	0,7514495	0,01949163	0,03406895
1,003681	1,057573	1,004565	1,121625	0,9550901	0,6370396	0	0,02523421
1,008968	1,035872	1,105052	1,263912	0,9058371	0,07630715	0	0,01673473
0,9961566	1	1,05701	1,183201	1,006406	0,06221475	0	0
0,9948755	0,9929538	0,950036	1,206262	0,9820642	0,1538154	0	0,02185924
0,9259089	1,049823	1,129246	1,062325	0,8508986	0,6821253	0,0268879	0,04012502
1,074091	1,054235	1,113435	1,099095	1,00239	0,7251459	0,00261985	0,01843085
1,003044	1,020669	1,133787	1,081875	0,9867014	0,7454036	0,0359303	0,00741037
0,9969558	0,9575406	1,019387	1,076107	0,9094732	0,7018226	0,0253555	0,0010014
1,261821	1,372582	1,189134	1,205946	1,001731	0,5651153	0,03751777	0
0,8449842	0,7223561	0,7955374	0,96514	0,716917	0,08399777	0,01427777	0
0,8731689	0,8993757	0,8360838	0,8257	0,6328574	0,01773904	0	0
1,020026	0,9710736	0,8939366	0,927066	0,6699425	0,04147352	0	0
0,9887581	1,004545	0,809726	0,9439104	0,5869224	0,05341366	0	0
1,041499	1,034682	0,9342233	0,9170018	0,7063968	0,04300898	0	0
0,9697427	0,9805062	0,7925044	0,9668725	0,6199303	0,01968816	0	0



SCP-1 N=3 n=4 (cell lines) Resazurin							
	THS [puff/ml]						
crl	$4 \cdot 10^{-5}$	$4 \cdot 10^{-4}$	$4 \cdot 10^{-3}$	$2 \cdot 10^{-2}$	$4 \cdot 10^{-2}$	$2 \cdot 10^{-1}$	$4 \cdot 10^{-1}$
1,029263	0,879564	0,9456545	1,119772	0,9395498	0,9055756	0,8673546	0,1541613
1,202585	0,9453891	1,026609	0,8824837	0,9143345	0,7404821	0,8017949	0,09497188
0,8580647	1,004313	0,9820176	0,6422753	0,9631725	1,390239	0,9257478	0,1058543
0,9100878	1,025282	1,134902	0,7593272	0,9095569	1,003251	0,8962857	0,09019426
1,103082	0,8395924	0,9773852	0,9479333	0,9237406	0,9368888	0,5295587	0,04044704
1,105974	1,118333	0,8863999	1,010256	0,957137	0,914274	0,6187032	0,04544334
0,8919221	0,9542444	0,8766702	0,8175035	0,8048813	0,8892925	0,7254664	0,01441367
0,8990221	0,8821924	0,921111	0,7015367	0,9061221	0,8077738	0,3751993	0,01152108
1,097499	1,001045	0,9428932	0,6796448	0,8520098	1,048053	0,4348517	0
0,8060458	1,12466	0,8189297	0,7454569	0,7343141	0,8446974	0,1851836	0,00272041
1,103767	0,7370998	0,7263052	0,8398224	0,8558401	0,6538771	0,6744217	0,00097935
0,9926875	0,9825894	0,8405188	0,5236458	0,4449498	0,6357701	0,8471349	0,00620253

SCP-1 N=3 n=4 (cell lines) Resazurin							
	Cigarette [puff/ml]						
crl	$4 \cdot 10^{-5}$	$4 \cdot 10^{-4}$	$4 \cdot 10^{-3}$	$2 \cdot 10^{-2}$	$4 \cdot 10^{-2}$	$2 \cdot 10^{-1}$	$4 \cdot 10^{-1}$
1,213328	0,9337775	1,193201	0,9643418	1,213328	0,8505335	0,00691112	0,01436581
1,026216	0,9056982	0,9688146	1,036404	0,8803523	0,7205734	0	0,00392924
0,8753824	1,612403	1,001118	0,9929181	0,9854634	0,7792169	0	0,00144435
0,8850735	0,851279	0,9862088	0,9742813	0,9464505	0,7302645	0	0
1,154861	0,9673204	1,102238	1,059131	1,007628	0,8774689	0	0
0,8497577	0,7145606	0,9510855	0,8304439	0,8452791	0,6694949	0	0
1,104757	0,9502458	1,072567	1,066409	1,380189	0,7212785	0,00162698	0
0,8906247	0,7621455	0,8449992	0,8738301	0,9639614	0,6006368	0	0
1,023121	0,7960556	0,7137096	0,7751618	0,6630116	0,3815605	0	0
1,009295	0,7533463	0,7650222	0,8320051	0,8575077	0,6796036	0	0,00393678
0,9542949	0,7877595	0,6322855	0,2912258	0,6181514	0,464521	0	0
1,013289	0,9423118	0,3237954	0,3520634	0,5299675	0,2291591	0	0



Figure 3 Viability 14 – 21 days

hOB N=5, n=3 Resazurin					
14 days					
	Cigarette [puff/ml]				
crl	$4 \cdot 10^{-5}$	$4 \cdot 10^{-4}$	$4 \cdot 10^{-3}$	$2 \cdot 10^{-2}$	$4 \cdot 10^{-2}$
1,066584	1,285854	1,230234	1,323826	1,393351	1,18745
0,9489259	1,231839	1,359123	1,286122	1,249488	1,044122
0,9844906	1,041982	1,245476	1,374097	1,289598	1,064444
0,9501693	0,9918965	0,9458152	0,8739719	0,9273101	0,7847121
1,086962	0,9842767	0,9795598	1,044872	0,9610547	0,7988631
0,9628689	0,9254959	1,048863	1,047412	0,2535075	0,6969037
1,097091	1,102264	0,9324486	0,9135553	0,5718998	0,5093717
0,9124306	1,052107	0,9216524	0,8703704	0,6153097	0,4266007
0,9904783	1,080897	0,8307842	0,9452692	0,614185	0,4695607
0,9995232	1,013112	0,9930862	1,042436	0,998808	0,5560853
0,9816426	0,9616164	0,9594707	1,093217	1,076052	0,4137561
1,018834	0,9465967	0,9365836	1,086065	0,9001073	0,4266301
1,030363	0,8561056	0,6594059	0,8613861	0,8415841	0
1,019802	0,9617162	0,7848185	1,010561	0,9656765	0,0640264
0,949835	1,162376	0,6462046	1,207261	0,8257425	0

hOB N=5, n=3 Resazurin					
14 days					
	THS [puff/ml]				
crl	$4 \cdot 10^{-5}$	$4 \cdot 10^{-4}$	$4 \cdot 10^{-3}$	$2 \cdot 10^{-2}$	$4 \cdot 10^{-2}$
1,041552	1,00212	1,192707	1,248887	1,197371	1,210727
1,000636	1,016112	1,149883	1,209667	1,267755	1,245919
0,9578122	0,9798601	1,313335	1,369091	1,155183	1,058088
0,9774644	1,084729	1,041294	1,083218	1,106257	0,954803
1,134206	1,079063	1,061312	1,076797	0,9427168	0,980486
0,8883293	0,8199673	0,8792648	0,8596248	0,8547148	0,7519829
0,8653846	1,094586	1,123432	1,065426	1,039402	1,073265
1,087061	0,9929975	1,216242	1,225021	0,940949	1,01181
1,047554	1,15949	1,160431	0,9334239	1,132839	0,9205686
1,100063	0,6324732	0,7891756	0,7319068	0,7369415	1,010069
0,9955947	0,6148521	0,7306482	0,7438641	0,7709251	0,8980491
0,9043424	0,6349906	0,7325362	0,7432348	0,7438641	0,9987413
0,8470948	0,4816514	0,8883792	0,7217125	1,238532	1,301223
1,131498	0	1,136086	1,149847	1,584098	1,56422
1,021407	0,3348624	0,9220183	0,7920489	1,530581	1,547401



hOB N=5, n=3 Resazurin					
21 days					
	Cigarette [puff/ml]				
crl	$4 \cdot 10^{-5}$	$4 \cdot 10^{-4}$	$4 \cdot 10^{-3}$	$2 \cdot 10^{-2}$	$4 \cdot 10^{-2}$
0,8836331	0,5658274	0,8793166	0,4703237	0,3899281	0,01600719
0,9839928	1,199281	1,18687	1,349281	1,432374	0,02086331
1,132374	1,119424	1,34982	1,30018	0,4384892	0,01546763
1,050399	0,9193616	0,6598068	1,211676	0,7820244	0
1,097018	1,113398	0,5892482	1,298614	0,7870643	0,03737925
0,8525829	0,8273835	1,279714	1,340193	0,6358673	0
0,8818933	1,446528	1,082831	0,8999777	0,6983702	0
0,9341371	1,199375	1,060728	0,92476	0,676267	0,1652154
1,18397	1,198035	1,081491	1,027908	0,8551016	0,2335343
0,976537	0,7989067	0,5409373	0,9223635	0,9223635	0
0,989067	1,084884	0,8084884	1,061298	1,061298	0,0334746
1,034396	0,9603218	1,01339	0,982802	0,982802	0,07769793
0,8572102	0,6712819	0,9142884	0,9357634	0,9357634	0
1,11378	1,023924	0,9301121	1,058397	1,058397	0
1,02901	1,057267	0,9261562	1,210417	1,210417	0

hOB N=5, n=3 Resazurin					
21 days					
	THS [puff/ml]				
crl	$4 \cdot 10^{-5}$	$4 \cdot 10^{-4}$	$4 \cdot 10^{-3}$	$2 \cdot 10^{-2}$	$4 \cdot 10^{-2}$
1,034078	1,196691	1,218546	1,250031	1,017039	1,039264
0,9307322	1,075935	1,404494	1,215212	1,00852	1,087048
1,03519	1,134461	1,42746	1,54303	1,384492	1,105939
0,8580462	1,095508	1,089621	0,8194505	0,9849542	0,9849542
1,14915	0,9241169	1,223724	0,7527257	0,3883559	1,0785
0,9928042	1,03925	1,0314	0,7847798	0,7108591	0,9064544
0,9191099	0,84411	0,9960733	0,6662304	0,6854712	0,8115183
1,0589	0,9104712	0,8755236	0,6524869	0,6980367	0,6748691
1,02199	1,096204	0,8818063	0,5445026	0,6171466	0,6732984
1,022671	0,5969861	0,8478363	0,8990465	1,248316	1,391945
0,8102287	0,3697406	0,5677802	0,7430153	0,9278522	1,385944
1,1671	0,3997466	1,009469	0,7610189	0,9606588	1,155898
0,9405495	0,1938147	0,6514037	1,372016	1,732322	1,067557
0,8621829	0,5613272	1,193665	1,467497	1,214382	1,320673
1,197268	0,5685332	1,49362	1,687284	1,698994	1,538658



SCP-1 N=3, n=3 Resazurin					
14 days					
	Cigarette [puff/ml]				
crl	$4 \cdot 10^{-5}$	$4 \cdot 10^{-4}$	$4 \cdot 10^{-3}$	$2 \cdot 10^{-2}$	$4 \cdot 10^{-2}$
0,9961109	0,8518385	0,7827603	0,7292556	0,4622461	0,07090638
1,018829	1,019497	0,999606	0,8696219	0,5332774	0,02372357
0,9850605	0,9768369	0,9217903	0,9112538	0,6712794	0,1191171
0,987513	0,9182418	1,088871	0,975105	0,8403562	0,5770624
0,9782268	1,02857	1,038528	0,9207708	0,6988106	0,528695
1,03426	1,056626	1,071208	1,019876	0,8920428	0,6261015
1,137154	1,074571	1,178931	0,9065334	0,4805009	0,02633574
0,9193363	1,103714	1,111548	0,9550496	0,3671281	0,02667266
0,9435101	1,028161	0,946037	0,7454867	0,4921246	0,00982677

SCP-1 N=3, n=3					
14 days					
	THS [puff/ml]				
crl	$4 \cdot 10^{-5}$	$4 \cdot 10^{-4}$	$4 \cdot 10^{-3}$	$2 \cdot 10^{-2}$	$4 \cdot 10^{-2}$
1,024798	0,8786517	0,8964553	0,8524843	0,8727824	0,836735
0,9979947	0,9229162	0,8772333	0,8902926	0,9800443	0,9566648
0,9772075	1,003424	0,9871364	1,049547	1,031254	0,9701643
0,9651753	0,8877481	0,9593621	0,9868129	0,9377649	0,9881451
1,0204	1,003001	0,97555	0,9541143	0,8878692	1,000417
1,014425	0,8260647	0,9880643	1,00954	1,077481	0,959887
0,954219	0,7710949	0,8530073	0,834869	0,8186897	0,7854604
0,96931	0,8767322	0,8674454	0,7570921	0,6797504	0,693608
1,076471	0,8823188	0,8202133	0,7929333	0,8360299	0,7766089

SCP-1 N=3, n=3 Resazurin					
21 days					
	Cigarette [puff/ml]				
crl	$4 \cdot 10^{-5}$	$4 \cdot 10^{-4}$	$4 \cdot 10^{-3}$	$2 \cdot 10^{-2}$	$4 \cdot 10^{-2}$
0,9669711	1,149538	1,068832	0,9648902	0,6084752	0,04506796
1,042426	1,162915	1,128482	0,9558734	0,5393127	0,00498737
0,9906033	1,148448	1,169554	1,074926	0,6049576	0,01459878
1,00423	1,050826	0,9513454	0,9187436	0,5860636	0,4117406
1,006873	0,979965	1,014316	0,8747907	0,5042985	0,4168393
0,988897	1,050491	1,029984	0,879666	0,5635847	0,4856158
1,172322	1,652221	1,555459	1,473039	0,6132618	0,01173439
1,042126	1,52007	1,415391	1,471735	0,3268867	0
0,7855524	1,024245	1,143638	1,205104	0,5764753	0,04153603



SCP-1 N=3, n=3 Resazurin					
21 days					
	THS [puff/ml]				
crl	$4 \cdot 10^{-5}$	$4 \cdot 10^{-4}$	$4 \cdot 10^{-3}$	$2 \cdot 10^{-2}$	$4 \cdot 10^{-2}$
1,016174	1,150157	1,225551	1,259723	1,090308	1,088106
0,9718691	1,159723	1,343172	1,258402	1,21781	1,145878
1,011957	1,172247	1,34078	1,426054	1,14915	1,266331
0,9644663	1,07185	1,09317	1,062271	1,001665	1,038528
1,005057	1,02634	1,079007	1,1171	0,97084	0,9262614
1,030477	1,084225	1,09317	1,106514	1,042479	1,167008
1,130073	0,908396	0,8786589	1,168945	1,30225	1,270741
0,9482941	1,0472	0,8342863	1,325368	1,150861	1,247623
0,9216332	0,8524641	0,6189485	0,9892176	0,966938	1,138835



Figure 4 Function 14-21 days

hOB N=5, n=3 - AP activity 14 days					
	Cigarette [puff/ml]				
crl	4.10^{-5}	4.10^{-4}	4.10^{-3}	2.10^{-2}	4.10^{-2}
1,263651	1,369763	1,879872	0,4974815	0,2418252	0,2450629
0,6940255	0,7584295	1,194501	0,6549677	0,1593495	0,6307492
1,042323	0,6761402	1,15593	0,4124046	0,1900225	0,4028788
0,9095936	0,7453535	0,8642386	0,1668019	0,6288301	0
0,9819286	0,8780741	0,8185215	0,2142623	0,2979579	0
1,108478	0,6469395	0,7644379	0,3926901	0	0,09712049
0,9358003	0,7308441	0,6969027	0,3813238	0,02928501	0
0,9820176	0,7561347	0,8304517	0,2559251	0,1660357	0
1,082182	0,6476755	0,8789489	0,2675388	0,06817202	0
1,311117	1,293531	1,528664	0,4605376	0,2208411	0,909989
0,912029	0,7960918	0,8519651	0,2967198	0,2532206	0
0,7768539	1,35701	1,537763	0,9677032	2,753291	1,06446
0,9939107	1,612294	1,931181	1,27159	0,4126738	0
1,021668	2,027856	1,463728	0,4494148	0,1567679	2,364447
0,9844212	0,9269973	1,612336	0,6712435	0,09705941	0

hOB N=5, n=3 - AP activity 14 days					
	THS [puff/ml]				
crl	4.10^{-5}	4.10^{-4}	4.10^{-3}	2.10^{-2}	4.10^{-2}
1,06072362	0,89893009	0,94767095	0,51716631	0,75234464	0,42817699
1,078617	1,288009	1,071653	0,5550102	0,911682	0,5388614
0,8606591	1,283623	1,210057	0,7697138	0,8901726	0,6586155
0,8214987	0,9789475	0,8360044	0,6685525	0,5223466	0,3458303
0,9957918	0,8589029	0,9263015	0,7875327	0,4457905	0,5893502
1,18271	0,6360809	0,7980241	0,8555417	0,6497324	0,3492884
1,064398	0,9650974	0,9489172	0,665038	0,5236611	0,3901069
1,176207	0,8984188	0,9003394	0,594172	0,5476475	0,3851532
0,7593948	0,8110788	1,426564	0,9868118	0,56576	0,4128318
0,1489946	0	0	3,060518	1,705146	5,787613
0	2,043732	4,860399	5,067834	5,03168	3,10268
3,564396	10,5829	5,444533	3,601944	0	3,008683
1,154161	0,7110966	0,7079812	0,8369629	0,3972085	0,4067858
0,5228394	0	0,1260711	0,6986318	0,2712475	0,2587702
1,323	1,171583	0,682151	0,668291	1,045624	0,07646269



hOB N=5, n=3 - Matrix formation 21 days					
	Cigarette [puff/ml]				
crl	$4 \cdot 10^{-5}$	$4 \cdot 10^{-4}$	$4 \cdot 10^{-3}$	$2 \cdot 10^{-2}$	$4 \cdot 10^{-2}$
1,415385	1,138462	1,046154	1,253846	1,207692	0,5153846
0,7692308	1,161538	1,138462	1,369231	0,8384615	0,8153846
0,8153846	1,115385	1,392308	1,023077	0,9307692	0,6076923
1,093333	1,373333	1,413333	1,013333	1,173333	0,4133333
0,9333333	1,373333	1,613333	0,9733334	1,133333	0,6133333
0,9733334	1,173333	0,9733334	0,9733334	0,9333333	0,5733333
1,253333	1,413333	1,013333	1,293333	0,7733333	0,4933333
1,013333	0,9333333	0,7733333	0,7733333	0,6533333	0,3333333
0,7333333	1,093333	0,7333333	0,7333333	0,6933333	0,2133333
0,9512195	1,243902	0,9512195	0,8780488	0,8048781	0,2926829
1,02439	0,8780488	0,8780488	0,9512195	0,8780488	0,2926829
1,02439	1,170732	0,8780488	1,170732	0,9512195	0
0,6	0,54	0,72	0,6	0,42	0
1,86	0,6	0,6	0,42	0,42	0
0,54	0,48	0,72	0,54	0,6	0

hOB N=5, n=3 - Matrix formation 21 days					
	THS [puff/ml]				
crl	$4 \cdot 10^{-5}$	$4 \cdot 10^{-4}$	$4 \cdot 10^{-3}$	$2 \cdot 10^{-2}$	$4 \cdot 10^{-2}$
0,97413793	1,05172414	1,18103448	1,4137931	1,18103448	0,94827586
0,8965517	1,155172	1,051724	0,9224138	1,025862	1
1,12931	1,12931	1,103448	1,232759	1,103448	0,9741379
1,166667	1,02381	1,059524	1,130952	1,452381	1,02381
0,8809524	1,130952	1,27381	1,27381	1,452381	1,130952
0,952381	0,952381	1,380952	1,02381	1,27381	1,059524
0,8915663	1,108434	0,9638554	1,144578	1,036145	1,036145
0,8554217	1,072289	1,180723	1,325301	1,072289	0,8915663
1,253012	0,8915663	1,036145	0,7469879	1,180723	0,7469879
0,862069	0,5724138	1,275862	1,193103	0,9448276	1,151724
0,862069	0,9448276	0,8206897	1,275862	1,027586	1,234483
1,275862	0,7793103	1,193103	0,862069	1,027586	1,027586
0,8245614	0,4035088	1,140351	1,035088	1,561404	1,140351
1,350877	0,4035088	1,350877	1,45614	1,666667	1,350877
0,8245614	1,982456	1,140351	1,245614	1,350877	1,77193



SCP-1 N=3, n=3 - AP activity 14 days					
	Cigarette [puff/ml]				
crl	$4 \cdot 10^{-5}$	$4 \cdot 10^{-4}$	$4 \cdot 10^{-3}$	$2 \cdot 10^{-2}$	$4 \cdot 10^{-2}$
0,8751697	1,381581	1,04062	0,9513543	0,3320031	0,9989368
0,9430035	0,9548556	1,329967	0,7758666	0,6096191	1,913898
1,181827	0,9965554	1,193986	0,9706179	0,3895991	1,661923
0,9509751	1,108688	1,229487	0,7454984	0,3483633	0,1995038
1,131492	0,8314677	0,8472497	0,7251875	0,3906829	0,1897581
0,9175333	0,9774941	0,8628564	0,5773129	0,4056139	0,3336067
1,123164	0,8963035	1,003442	0,6033995	0,1579597	0
1,039109	0,986459	1,149037	0,770057	0,07841832	0,4906211
0,8377276	0,6923893	0,9184857	0,5547019	0,2020929	1,331686

SCP-1 N=3, n=3 - AP activity 14 days					
	THS [puff/ml]				
crl	$4 \cdot 10^{-5}$	$4 \cdot 10^{-4}$	$4 \cdot 10^{-3}$	$2 \cdot 10^{-2}$	$4 \cdot 10^{-2}$
1,015683	0,9600994	1,051063	1,058994	0,8158679	0,5523747
0,8518772	0,9853028	0,9016824	0,9992493	0,8406409	0,4556326
1,13244	0,8800353	1,061095	0,7849724	0,7096241	0,4560708
1,176491	1,173565	0,976584	0,9190364	0,8911752	0,7812656
0,8777681	0,9004673	1,106357	1,033017	1,034116	0,8503484
0,9457409	1,451737	1,065794	1,135926	0,9843034	0,78084
1,00024	0,9036285	0,5615878	0,5042387	0,5585316	0,5174761
1,055803	0,7409392	0,7948917	0,7238103	0,539223	0,444735
0,943957	0,6622117	0,6504098	0,576674	0,5990372	0,5654309

SCP-1 N=3, n=3 - Matrix formation 21 days					
	Cigarette [puff/ml]				
crl	$4 \cdot 10^{-5}$	$4 \cdot 10^{-4}$	$4 \cdot 10^{-3}$	$2 \cdot 10^{-2}$	$4 \cdot 10^{-2}$
0,9670542	0,9786822	1,228682	1,094961	0,8624031	0,07751938
0,9612403	1,089147	1,141473	1,263566	0,6414729	0,00775194
1,071705	1,217054	1,193798	1,164729	0,5251938	0,124031
0,9808542	1,095729	1,162003	1,188513	0,9234168	0,4329897
1,038292	1,095729	1,166421	1,250368	0,7908689	0,6804124
0,9808542	1,11782	1,14433	1,157585	1,007364	0,4727541
1,087558	1,032258	0,8801844	0,7557604	0,3410138	0
0,797235	1,447005	0,921659	0,8525345	0,3963134	0,02304147
1,115207	1,198157	1,156682	1,004608	0,4101382	0,05069124



SCP-1 N=3, n=3 - Matrix formation 21 days					
	THS [puff/ml]				
crl	$4 \cdot 10^{-5}$	$4 \cdot 10^{-4}$	$4 \cdot 10^{-3}$	$2 \cdot 10^{-2}$	$4 \cdot 10^{-2}$
0,9854546	0,9472727	0,9363636	1,001818	1,023636	0,9036363
0,9145455	0,9690909	1,045455	0,9254546	0,9145455	0,9309091
1,1	0,9418182	0,9909091	0,8436363	0,8163636	0,7945455
0,9891697	1	0,9314079	0,8953069	0,9494585	0,8519856
1,075812	0,9277979	0,8953069	0,9169675	0,8628159	0,7833935
0,9350181	0,9133574	0,8916968	1,043321	0,9025271	0,8880866
1,037356	0,795977	0,8304598	0,7097701	0,6063218	0,7873563
0,9511494	0,7097701	0,658046	0,6666667	0,6494253	0,6321839
1,011494	0,6925287	0,7873563	0,7270115	0,7787356	0,7356322



Figure 5 Oxidative stress – Primary cilia

ROS - SCP-1 N=3, n=3				
	Cigarette [puff/ml]			positive ctrl
crl	$2 \cdot 10^{-2}$	$4 \cdot 10^{-2}$	$2 \cdot 10^{-1}$	H ₂ O ₂
0	12,24206	16,8912	23,46903	1,697553
3	9,799583	9,704321	19,20562	25,00729
0	2,993753	18,65591	20,3316	14,61739
0,8429304	0,9975138	0,8704257	1,130342	3,554361
1,15707	1,181086	0,5073468	0,9512962	3,626264
3,199172	0,5352952	0,5543606	0,907006	3,488323
1,186994	8,581155	0,4854465	9,145535	3,109152
0,9520923	18,24174	11,21214	16,42772	4,628865
0,860914	4,914652	11,13962	15,96695	4,382125

ROS - SCP-1 N=3, n=3				
	THS [puff/ml]			positive ctrl
crl	$2 \cdot 10^{-2}$	$4 \cdot 10^{-2}$	$2 \cdot 10^{-1}$	H ₂ O ₂
0,7362362	0,5894301	1,41619	1,915796	20,93537
1,154595	0,1369552	0	1,510846	19,52985
1,109169	0	0,375567	2,344804	45,47706
0	1,112345	1,412628	2,037897	6,224256
3	1,970237	0,8931836	2,243295	15,04356
0	1,412426	1,211213	1,952339	16,27152
0,346718	0	0	4,248852	12,15484
2,653282	3,378723	4,938509	9,386947	2,058786
0	0	0	4,16595	25,13234

Primary cilia length [µm] SCP-1 N=3, n=3					
	Cigarette [puff/ml]				
Crl	$4 \cdot 10^{-5}$	$4 \cdot 10^{-4}$	$4 \cdot 10^{-3}$	$2 \cdot 10^{-2}$	$4 \cdot 10^{-2}$
3,03370565	3,26412615	2,82141919	2,11892247	1,95354796	2,15519054
2,42306176	3,44921156	4,08843627	2,16721419	2,51057819	0
2,89395532	1,78738502	2,62805519	3,41649146	3,07884363	0
2,79382392	2,39802891	2,47943495	2,47943495	2,82141919	0
2,260841	1,82562418	2,70591327	3,16458607	1,71327201	0
2,89099869	2,95289093	4,12411301	3,35026281	4,3760184	0
1,60407359	2,51057819	3,60827858	2,05269382	3,35026281	0
2,80919842	4,04802891	1,95354796	4,04802891	3,86471748	0
2,23383706	3,16458607	3,62503285	1,86760841	2,1392247	4,0565046
3,58659658	3,25072273	3,99658344	2,03988173	3,60827858	2,17509855
2,93830486	3,56984231	4,29638633	1,57687254	0	1,8303548
2,89099869	3,02227332	3,83120894	2,32844941	0	2,69625493
3,68869908	1,94014455	2,52417871	4,53114323	0	3,0760841



Primary cilia length [µm] SCP-1 N=3, n=3					
Crl	Cigarette [puff/ml]				
	4.10 ⁻⁵	4.10 ⁻⁴	4.10 ⁻³	2.10 ⁻²	4.10 ⁻²
2,99940867	2,89099869	4,36813403	2,3653088	0	0
2,89395532	3,0760841	8,34816032	2,6412615	0	0
2,24546649	3,76281209	2,8848883	2,78436268	0	0
2,53777924	4,08212878	2,83659658	2,23777924	0	0
2,1392247	3,86708279	4,71051248	3,53830486	0	0
2,58173456	3,17838371	2,97339028	2,29868594	0	0
2,1065046	2,3653088	1,95354796	2,35072273	0	4,92555848
3,47917214	2,68009198	9,02503285	3,10131406	0	0
2,75952694	3,28521682	2,35072273	3,32424442	0	0
2,95289093	2,1392247	3,35026281	2,29494087	4,52542707	0
4,86386334	2,93830486	3,65341656	2,1392247	2,32844941	0
2,99645204	2,50013141	4,15545335	3,12339028	2,3653088	0
2,65742444	3,44921156	1,05946124	3,10131406	3,2956636	0
2,68009198	2,62805519	2,03988173	2,46898817	2,70591327	2,608346
2,01011827	3,02522996	5,45144547	2,23777924	1,83961892	0
3,72141919	2,00578187	2,1392247	2,6607753	2,80919842	0
3,06760841	1,78738502	3,76281209	3,32424442	2,29868594	0
3,63449409	2,05683311	3,19986859	3,78350854	2,04421813	0
3,0478975	3,68180026	5,05525624	3,41156373	2,44434954	0
2,97339028	2,33968463	2,78751643	2,52417871	2,88193167	2,7090688
2,69625493	2,70906702	4,24592641	2,59178712	2,23777924	2,62805692
3,07884363	1,60407359	4,4696452	2,6607753	4,79586071	0
3,25348226	2,91760841	3,06484888	4,9673456	2,91760841	0
0	3,73521682	3,57457293	2,42306176	4,28022339	1,83962013
0	2,81215506	4,49862024	4,12411301	2,29494087	0
0	2,99645204	1,49822602	3,35026281	2,49678055	0
0	1,83961892	2,65742444	2,20269382	2,62805519	
0	4,29027595	1,21143233	3,81070959	2,6607753	
0	3,20795007	3,81070959	3,99658344	3,70269382	
0	3,60827858	3,02522996	5,31662286	0	
0	0	2,95289093	0	0	
0	0	3,471682	0	0	
0	0	4,55578187	0	0	
0	0	5,68541393	0	0	
0	0	3,20795007	0	0	
0	0	5,15164258	0	0	
0	0	4,61412615	0	0	
0	0	3,22155059	0	0	
0	0	2,55137976	0	0	
0	0	2,88193167	0	0	
0	0	6,89605782	0	4,90978975	
0	0	0	0	2,41596583	



Primary cilia length [µm] SCP-1 N=3, n=3					
	Cigarette [puff/ml]				
Crl	4.10 ⁻⁵	4.10 ⁻⁴	4.10 ⁻³	2.10 ⁻²	4.10 ⁻²
0	0	0	0	4,76156373	
0	0	0	0	4,0565046	
0	0	0	0	4,25597898	
0	0	0	0	3,73521682	
0	0	0	0	4,32240473	
0	0	0	0	4,73061761	
0	0	0	0	3,41156373	
0	0	0	0	2,53777924	
0	0	0	0	4,07365309	
0	0	0	0	3,50637319	
0	0	0	0	2,91760841	
0	0	0	0	3,2956636	
0	0	0	0	2,33968463	
0	0	0	1,82562418	5,94973719	
0	2,88193167	0	3,00236531	4,40558476	
0	3,86471748	0	2,70906702	0	
0	6,05321945	0	2,11892247	0	
0	3,18094612	0	2,11892247	0	
5,72483574	2,52772668	0	2,75952694	0	
3,589159	2,35072273	0	1,32063075	0	
2,70591327	4,00308804	0	3,28777924	0	
3,99007884	3,58659658	0	2,3653088	0	
4,41721419	2,00578187	1,58239159	3,12339028	0	
3,62503285	2,45479632	2,53777924	2,99645204	0	
3,06760841	1,39691196	5,70512484	2,23383706	0	
3,17838371	1,46925099	3,3086728	2,93830486	0	
2,00144547	2,11892247	3,06484888	2,8304862	0	
4,41721419	2,62805519	2,83659658	2,46898817	0	
2,20269382	3,17838371	3,71668857	2,11892247	0	
7,25716163	2,3653088	2,18712221	2,29494087	0	
1,72844941	3,6652431	1,58771353	1,84434954	0	
3,36563732	7,16018397	1,70834428	1,70834428	0	
7,56701708	2,23383706	1,95354796	3,17838371	0	
2,64441524	3,42674113	3,53830486	2,95289093	0	
2,07772668	2,77194481	1,37187911	2,51057819	0	
3,35795007	3,1565046	2,3653088	1,7629435	1,498227	
4,81911958	2,20269382	3,63449409	1,88140604	2,93830679	
3,65105125	2,73429698	1,68272011	3,02522996	2,7090688	
3,15374507	2,29494087	3,35026281	4,32240473	2,51057984	
3,96189225	3,50637319	2,45479632	2,89395532	2,70591505	
4,33442838	2,55137976	2,260841	2,97910644	1,82562538	
2,79382392	2,52772668	2,41596583	2,42306176	3,63449647	



Primary cilia length [µm] SCP-1 N=3, n=3					
	Cigarette [puff/ml]				
Crl	4.10 ⁻⁵	4.10 ⁻⁴	4.10 ⁻³	2.10 ⁻²	4.10 ⁻²
3,99658344	2,77194481	2,42306176	2,62805519	2,36531036	
5,48298292	3,55762155	3,65341656	2,42306176	3,2321966	
3,15926413	2,91760841	3,82667543	4,19053876	1,97109197	
4,01156373	3,22155059	3,0478975	3,53830486	3,02523195	
3,20795007	3,06760841	2,23383706	3,58659658	1,31412701	
4,0586728	1,67247043	1,60407359	2,97910644	0	
6,57023653	3,3086728	2,61819974	4,34428384	0	
3,5260841	2,81215506	2,77194481	1,59855453	0	
2,70906702	3,15374507	2,47943495	4,48521682	0	
2,11892247	1,86760841	4,55578187	3,1151117	0	
2,96471748	1,32063075	3,5260841	2,07772668	0	
4,19881735	4,4696452	2,70591327	2,58843627	0	
2,26833114	2,68009198	2,61819974	2,70591327	0	
3,70052562	3,70269382	3,60827858	2,62805519	0	
5,1717477	2,49323259	1,85834428	2,97339028	0	
4,1761498	4,45998686	2,41596583	2,05269382	0	
3,42674113	4,59914586	3,73758213	3,35026281	0	
0	3,49888305	3,97706965	5,29060447	0	
0	3,02522996	3,71905388	3,439159	0	
0	2,93830486	4,73791064	3,55762155	0	
0	1,71327201	1,39691196	3,16458607	0	
0	3,62503285	4,73968463	2,53777924	2,49323423	
0	2,1392247	1,95354796	0	2,23778071	
0	2,41222076	3,02522996	0	3,42674338	
0	3,19730618	4,21320631	0	1,72845054	
0	3,45670171	5,23147175	0	2,05269517	
0	2,18712221	5,79520368	0	3,92030481	
0	0	0	0	3,1592662	
0	0	0	0	3,02227531	
0	0	0	0	4,73791376	
0	0	0	0	3,71669101	
0	0	0	0	1,91333897	
0	0	0	0	4,74875476	
0	0	0	0	2,91761033	
0	0	0	0	3,55033085	
0	0	0	0	0	
0	0	0	0	0	
0	0	0	0	0	
0	0	0	0	0	
0	0	0	0	0	
0	0	0	0	0	
0	0	0	0	0	



Primary cilia length [µm] SCP-1 N=3, n=3					
	Cigarette [puff/ml]				
Crl	4.10 ⁻⁵	4.10 ⁻⁴	4.10 ⁻³	2.10 ⁻²	4.10 ⁻²
0	0	0	0	0	
2,91760841	2,41596583	0	0	0	
8,17884363	2,23383706	0	0	3,20795217	
5,8086071	2,52772668	0	0	2,81215691	
2,89395532	4,62910644	0	0	2,20269527	
4,10519054	2,8304862	0	0	1,68272121	
4,00525624	3,20795007	0	0	3,79257805	
2,58843627	3,71668857	0	0	2,88193356	
3,439159	3,94434954	0	2,37989488	2,23778071	
3,19986859	5,14001314	1,70834428	3,37844941	3,22155271	
4,53114323	4,64408673	3,36819974	3,17838371	3,15650667	
3,62503285	2,41596583	2,6607753	4,21320631	4,61610027	
4,08212878	3,81977661	4,58416557	1,95354796	2,7626825	
3,50637319	2,55137976	2,51057819	1,95354796	2,16721562	
2,6607753	3,64395532	4,95354796	4,0565046	2,88193356	
3,42674113	4,4696452	1,57687254	5,19835742	2,33968616	
3,1151117	3,00236531	3,84678055	1,31412615	2,36531036	
3,10131406	4,19053876	3,66051248	4,22345598	2,42306335	
2,68009198	3,66051248	3,31655716	2,05683311	2,75952875	
3,5260841	3,45670171	3,19730618	3,63449409	2,23383852	
2,36905388	3,86471748	4,95354796	2,23009198	2,16721562	
4,93955322	3,19986859	3,41156373	3,79040736	0	
2,59178712	4,20492773	2,62805519	4,03088042	0	
2,83659658	3,06760841	2,29494087	3,66051248	0	
3,79257556	1,60407359	3,45670171	3,68869908	0	
2,58173456	3,46931669	1,8303548	7,58061761	0	
3,3912615	2,37989488	4,23764783	4,04802891		
3,32424442	3,20795007	4,24592641	2,82141919		
8,27956636	2,6412615	2,95289093	3,68180026		
4,81202365	4,56149803	3,22155059	2,41596583		
2,93830486	4,58988173	3,0760841	9,85900131		
3,37844941	3,53574244	3,71905388	4,23153745		
3,55032852	3,66051248	2,70906702	3,35026281		
2,55137976	3,49888305	2,86990802	3,26412615		
4,20709593	2,88193167	3,15374507	3,92030223		
3,42674113	2,36905388	3,37844941	3,73521682		
2,23777924	3,76281209	3,73994744	2,84270696		
3,63449409	1,88140604	1,67247043	1,97109067		
2,8848883	4,81911958	2,60834428	1,58239159		
0	3,81977661	4,20492773	4,32240473		
0	3,439159	2,49323259	4,14914586		
0	3,44921156	4,12628121	3,25072273		



Primary cilia length [µm] SCP-1 N=3, n=3					
	Cigarette [puff/ml]				
Crl	4.10 ⁻⁵	4.10 ⁻⁴	4.10 ⁻³	2.10 ⁻²	4.10 ⁻²
0	2,84270696	2,59178712	3,49888305		
0	3,73521682	3,96189225	2,53777924		
0	4,94645204	3,19730618	3,94434954		
0	3,72141919	3,61537451	3,23219448		
0	1,85834428	3,84678055	3,15926413		
0	3,97273325	6,14388962	3,44921156		
0	2,99645204	4,56149803	1,86760841		
0	2,24921156	4,76156373	3,89152431		
0	0	5,65663601	2,260841		
0	0	4,88337714	2,52417871		
0	0	3,64395532	3,62503285		
0	0	3,92030223	5,02963206		
0	0	2,78751643	2,91760841		
0	0	2,91760841	3,12339028		
0	0	3,53830486	0		
0	0	4,20709593	0		
0	0	5,49086728	0		
0	0	2,26833114	0		
0	0	3,07884363	0		
0	0	1,97109067	0		
0	0	0	0		
0	0	0	0		
1,70834541	0	0	0		
3,63449647	0	0	0		
1,46925195	0	0	0		
2,93830679	0	0	0		
1,34014543	0	0	0		
2,1025638	0	0	0		
4,38587673	0	0	0		
4,53883347	0	0	0		
2,73429877	0	0	0		
3,62503523	0	0	0		
2,65742619	0	0	0		
2,16721562	2,44435115	0	0		
4,18226293	2,05683447	0	0		
2,62805692	3,03370764	0	0		
2,99645401	3,57457528	0	0		
3,92030481	1,71327314	0	0		
2,07772804	2,70591505	0	0		
1,31412701	2,42306335	0	2,66077704		
1,31412701	1,42135442	0	2,6962567		
2,18712364	2,29494238	3,28521898	3,66051489		



Primary cilia length [µm] SCP-1 N=3, n=3					
	Cigarette [puff/ml]				
Crl	4.10 ⁻⁵	4.10 ⁻⁴	4.10 ⁻³	2.10 ⁻²	4.10 ⁻²
1,88140728	2,88193356	2,93830679	4,46196088		
2,45479793	1,72845054	5,31662636	2,89100059		
2,59178883	1,39691288	7,18423599	1,8583455		
3,02523195	2,75952875	1,64645312	1,89520492		
2,62805692	1,21143312	3,00236728	1,88140728		
3,13443044	2,4689898	1,532524	3,16458815		
1,76787238	3,42674338	1,76294465	2,608346		
2,58843797	2,49678219	3,65341896	3,92030481		
2,64441698	1,58239263	1,88140728	2,10650598		
0	1,8583455	3,12339233	3,41156597		
0	2,55138144	2,7626825	4,8352857		
0	1,58239263	2,77194663	4,49093593		
0	3,49888535	2,01011959	3,03370764		
0	5,8190577	2,70591505	3,4164937		
0	2,55138144	3,47168428	2,9791084		
0	3,79040985	3,71905632	0		
0	4,27825511	3,83121145	0		
0	1,8583455	2,70591505	0		
0	2,61820146	3,53830719	0		
0	0	1,830356	0		
0	0	2,36531036	0		
2,32490297	0	2,36905543	0		
1,32063162	0	2,29494238	0		
2,13922611	0	3,16458815	0		
3,71669101	2,36905543	1,82562538	0		
0,84145916	2,58173626	2,13922611	0		
4,47556142	3,03370764	1,13042124	0		
3,53830719	3,63449647	3,29310335	0		
1,67247153	1,97109197	2,63140777	0		
2,26084248	3,19730828	2,04421948	0		
3,35795227	3,92030481	1,67247153	0		
3,89152687	3,57457528	3,13443044	0		
1,58771458	1,76787238	3,76281456	0		
2,12286605	3,0928404	2,23778071	2,26833263		
2,59178883	1,78738619	3,03370764	2,41596742		
3,12339233	1,95354925	0	5,03653419		
2,23009345	2,36905543	0	2,05269517		
3,97707226	4,2802262	0	1,71327314		
2,89395722	1,64645312	0	1,498227		
3,35026501	3,47168428	0	2,26084248		
2,88193356	1,67247153	0	2,44435115		
2,23778071	0,95657093	0	3,1013161		



Primary cilia length [µm] SCP-1 N=3, n=3					
	Cigarette [puff/ml]				
Crl	4.10 ⁻⁵	4.10 ⁻⁴	4.10 ⁻³	2.10 ⁻²	4.10 ⁻²
2,36905543	2,05269517	2,96471942	2,89395722		
1,97109197	3,94218393	2,64126323	2,41596742		
2,53778091	3,31655934	1,8583455	2,49678219		
3,83791317	1,78738619	1,46925195	2,75952875		
2,8848902	2,41596742	3,17838579	6,34297394		
3,16458815	2,7626825	2,63140777	1,532524		
1,82562538	2,13922611	3,11511374	1,58239263		
2,97339223	4,53114621	1,95354925	4,81912275		
3,04789951	1,78738619	2,1025638	1,86760964		
3,25072487	2,1025638	1,98843757	2,52418037		
3,15374714	0	3,1998707	1,83962013		
3,43916126	0	3,78351103	1,18265518		
0	0	1,83962013	2,66077704		
0	0	1,41524403	2,11892386		
0	0	2,59178883	2,89395722		
0	0	1,84435075	1,71327314		
0	2,62805692	2,41596742	3,12339233		
0	4,64960884	2,89100059	2,29868745		
0	4,46393197	4,8780584	5,93653478		
0	3,1592662	3,81977912	2,17509998		
0	4,17615255	3,17838579	1,88140728		
0	3,2534844	3,3242466	3,90690138		
0	2,03988307	3,34514017	3,34514017		
1,39691288	3,54796554	2,1025638	3,00236728		
2,00144678	1,41524403	2,17509998	4,09257825		
1,70834541	3,42674338	2,11892386	2,13922611		
3,47168428	2,73429877	2,23778071	0		
2,78436451	2,88193356	3,16458815	0		
5,07575892	1,89520492	2,47943658	0		
1,83962013	1,88140728	1,88140728	0		
1,59855558	2,55138144	2,10650598	0		
2,66077704	2,99941064	0	0		
2,32490297	3,68180268	0	0		
2,49323423	2,7090688	0	0		
1,83962013	2,33968616	3,63449647	0		
1,31412701	2,89395722	2,82142104	0		
3,58916136	3,32700613	3,72142163	0		
3,26412829	2,26084248	2,8848902	0		
3,06761043	1,58239263	2,62805692	0		
1,532524	0	3,47917443	0		
3,07608612	0	3,40900355	0		
3,28521898	0	1,84435075	3,55033085		



Primary cilia length [µm] SCP-1 N=3, n=3					
	Cigarette [puff/ml]				
Crl	4.10 ⁻⁵	4.10 ⁻⁴	4.10 ⁻³	2.10 ⁻²	4.10 ⁻²
2,77194663	0	4,35236817	1,05118335		
1,64645312	0	2,42306335	3,1998707		
2,55138144	0	1,91333897	2,36905543		
1,82562538	0	2,6962567	1,67247153		
3,16458815	0	1,53804306	3,97273586		
2,07772804	0	2,93830679	2,62805692		
1,97542837	0	2,01011959	3,1013161		
2,32845094	0	2,62805692	1,97542837		
1,91333897	0	2,29868745	2,9791084		
2,70591505	0	2,55138144	3,06761043		
1,53804306	0	2,52772834	3,32700613		
4,24178991		3,81977912	2,89100059		
0		3,35795227	2,52418037		
0		4,29027877	4,3681369		
0		4,04803157	3,92030481		
0		3,46931897	2,7626825		
0		6,11294751	3,16458815		
0		1,95354925	2,13922611		
0		1,97109197	2,58173626		
0		2,90874041	3,15650667		
		1,60407464	1,62536243		
		3,1998707	1,53804306		
		2,89100059	3,20795217		
		2,84270883	1,44540174		
		2,99645401	2,12286605		
		3,19730828	2,95289287		
		2,8848902	1,21143312		
		1,31412701	1,83962013		
		2,23383852	3,76281456		
		2,4689898	2,55138144		
		2,37989644	1,57687357		
		3,03370764	2,64126323		
		0	1,88140728		
		0	0		
		0	0		
		0	0		
		0	0		
		0	0		
		0	0		
		0	0		
		0	0		



Primary cilia length [µm] SCP-1 N=3, n=3					
Crl	THS [puff/ml]				
	4.10 ⁻⁵	4.10 ⁻⁴	4.10 ⁻³	2.10 ⁻²	4.10 ⁻²
2,11475271	1,8407201	4,39691515	3,07278487	2,22570346	5,74799623
1,78386768	2,99055542	0,99875344	3,60117797	2,39330991	2,32032635
2,36439189	4,1159973	2,00183475	2,91186694	1,18760578	4,00366951
2,00183475	2,60321141	2,94708003	9,89271482	1,49527771	4,26983327
2,5056377	4,48976755	3,1910143	6,79179883	3,85711222	3,22583395
3,94307938	3,40976826	2,65219498	7,95678167	2,62288353	2,63921138
3,83035814	1,31154012	3,54334194	3,46485019	2,58668683	1,99750689
2,18281824	3,8122598	4,75042311	0,74183558	2,1629494	5,26720966
4,30189882	2,72891624	4,07193176	3,46248953	2,23337558	5,72852083
2,36439189	5,40727514	3,43239119	4,19881692	2,75724409	2,70058839
4,39888236	3,49947312	3,41232563	1,89147417	2,4182935	2,95888331
4,43783316	4,96465248	2,78203096	5,37855385	1,31803192	0,6556717
3,36157157	3,75776803	4,46675117	1,17304841	2,83711289	0
2,94708003	1,39416302	2,13501499	1,31803192	2,22570346	0
2,03586752	3,52878457	2,61304747	1,60091698	4,52222654	0
3,75540737	2,83101454	2,73835886	2,17081825	3,46248953	0
2,60321141	5,63330778	3,44242397	3,89271876	3,31770274	0
1,98452329	2,29042473	3,07003077	3,48471903	2,29416243	0
2,5056377	2,49186722	2,87921123	4,42425939	1,31154012	0
2,70373593	3,17468644	3,35134206	2,52275244	3,17212907	0
2,75409655	3,64386646	3,40229285	4,85252141	3,25770278	0
2,22944116	3,22583395	2,73835886	0,92734365	3,51914523	0
1,78386768	3,15835858	3,49947312	4,66996415	1,7496382	0
4,39888236	2,95888331	2,76648999	4,10773501	5,43422594	0
4,51652163	2,15094941	2,36439189	4,38314467	2,77888342	0
1,64321204	2,00183475	2,1629494	3,28130932	3,49199771	0
1,33750732	4,48976755	2,34609682	1,70498249	2,87626041	0
3,27875195	3,15835858	3,28130932	3,75540737	3,17212907	0
3,05035866	3,81914504	2,93252267	3,27875195	3,1910143	0
7,38629024	3,67455497	2,83101454	2,70373593	3,11724386	0
3,67455497	6,0328485	2,87921123	2,86426042	4,65166908	0
1,53501539	3,78511227	4,89658695	5,18812775	1,23717952	0
3,60117797	2,54635899	3,41999776	6,80950373	5,41691448	0
3,28917817	3,75776803	3,12826024	4,99907869	1,82203159	2,59652289
1,8359988	3,21521101	2,96753904	4,59757076	0	1,85468731
1,98452329	4,98530821	2,94708003	3,49947312	0	1,99750689
3,53134195	2,87626041	4,00366951	0	0	1,89147417
2,25639196	3,64386646	3,8122598	0	0	3,61789927
3,68144021	3,96491543	3,37180107	0	0	3,55062062
2,22570346	3,55062062	4,30189882	0	0	1,17304841
2,87921123	4,20491528	1,70990052	0	0	3,11724386
2,03586752	3,58209601	2,91186694	0	0	4,07409569



Primary cilia length [µm] SCP-1 N=3, n=3					
	THS [puff/ml]				
Crl	4.10 ⁻⁵	4.10 ⁻⁴	4.10 ⁻³	2.10 ⁻²	4.10 ⁻²
1,31154012	2,23337558	3,31003062	0	0	3,15304711
1,90957252	3,57953864	4,45907904	0	0	3,02773572
6,62773336	2,93252267	4,29599718	0	0	1,29167128
1,23717952	3,07003077	2,65219498	0	0	0
1,39416302	2,22570346	3,06157176	0	0	0
3,85947288	0	2,24104771	0	0	0
0	0	2,67481792	0	0	0
0	0	0	0	0	0
0	0	0	0	0	0
0	0	0	0	0	0
0	0	0	0	0	0
0	0	0	0	0	0
0	0	0	0	1,20904839	0
0	0	0	0	3,65330908	0
0	0	0	0	2,99350623	0
0	0	0	0	4,19881692	0
0	0	0	0	3,20163724	0
0	0	0	0	1,36917943	0
0	0	0	0	3,40229285	0
0	0	0	0	4,46675117	2,65553924
0	0	0	0	3,15835858	2,05278554
0	0	0	0	1,29167128	2,97324395
0	0	0	0	2,96753904	1,87770369
0	0	0	0	3,49199771	3,87501385
0	0	0	0	2,00616262	3,62734188
0	0	0	0	2,75409655	6,37376631
0	3,69324348	0	0	3,07003077	3,12826024
0	4,80963619	0	0	2,93252267	2,80662111
0	5,3529801	0	0	2,70373593	4,10773501
0	4,29599718	0	3,06157176	2,61304747	0
0	5,82097979	0	2,10235928	3,2866208	0
2,93252267	1,98452329	0	1,8359988	2,07363798	0
2,48832624	1,20904839	0	2,52275244	2,19835921	0
2,34609682	4,32786601	0	2,69094906	3,64386646	0
3,06157176	3,65803039	0	3,78294834	2,29042473	0
0,99875344	2,09842485	2,11475271	3,36157157	0	0
2,04865439	5,66360284	3,12826024	1,76439229	0	0
2,8882604	3,35134206	4,00366951	4,04006292	0	0
3,28917817	2,93252267	3,49947312	3,41999776	0	0
3,23901427	3,15835858	2,70373593	2,07363798	0	0
3,55062062	3,2866208	4,45907904	3,7760631	0	0
3,69540741	4,73763624	3,01927671	1,8267529	0	0
1,29167128	3,8392106	2,4182935	1,70498249	0	0



Primary cilia length [µm] SCP-1 N=3, n=3					
	THS [puff/ml]				
Crl	4.10 ⁻⁵	4.10 ⁻⁴	4.10 ⁻³	2.10 ⁻²	4.10 ⁻²
1,99750689	4,59009535	4,07409569	1,78386768	0	2,77194663
1,59540879	5,18812775	2,78832604	2,09842485	0	3,17838579
2,94708003	2,65553924	4,01232524	3,07003077	0	2,6962567
4,19881692	5,04530817	2,78832604	2,78832604	0	3,24540292
3,02773572	2,17081825	2,15094941	3,46248953	0	3,03370764
2,4182935	2,29416243	3,70937462	2,86426042	0	2,1025638
3,32045684	3,69324348	2,00183475	2,89711285	0	3,78351103
2,94708003	4,76852146	2,15094941	3,28917817	0	2,32490297
3,49199771	4,75219361	3,57953864	1,57927765	0	1,94014582
1,59540879	3,1910143	1,41855645	2,67481792	0	3,20795217
6,03855342	3,67455497	3,27875195	3,11724386	0	2,64441698
3,40976826	5,01107868	3,15835858	3,73258772	0	3,1592662
3,53134195	3,05881767	2,83101454	1,05737636	0	2,49323423
2,34609682	3,75540737	3,48471903	2,33508044	0	1,60407464
4,61999697	2,87626041	2,52275244	2,15094941	3,61789927	2,60164428
2,54635899	4,19881692	3,62734188	3,73258772	2,4182935	2,65742619
2,81586701	4,06760389	2,65219498	2,75724409	2,41121153	0
2,49186722	5,87232402	5,16668514	3,17468644	5,80760275	0
1,60091698	3,72786641	2,13501499	3,32045684	2,25639196	0
2,58668683	2,96753904	4,14098089	3,32045684	3,85711222	0
1,65894973	2,63606385	2,78832604	1,70990052	1,78386768	0
2,5056377	3,07003077	5,24596377	2,48832624	2,32386733	0
3,40976826	4,27180048	2,24104771	5,67422579	4,11816123	0
2,10235928	2,4182935	3,51914523	2,78832604	3,46248953	0
4,72858706	2,48832624	2,22944116	2,07363798	3,16937497	0
3,62734188	2,65219498	3,62734188	1,70498249	1,82203159	1,84435075
4,7085215	2,58668683	6,21402871	3,96491543	1,89147417	2,99645401
4,27180048	3,62734188	3,9692433	6,09658617	2,87921123	1,66222185
2,67481792	3,81914504	3,54098128	4,09711207	1,99750689	2,05683447
2,23337558	3,60117797	3,71409593	2,62288353	3,88386631	2,42306335
6,95074954	4,7539641	3,40976826	2,62622779	3,95409577	1,83962013
4,07409569	1,57927765	2,17081825	0	2,22570346	2,00144678
4,77383294	0	2,82491618	0	3,75540737	1,82562538
2,91186694	0	3,9887187	0	3,43239119	3,88029164
6,26911064	0	6,49415968	0	2,72891624	1,89520492
4,75219361	0	2,15094941	0	2,86426042	1,46925195
3,43239119	0	5,75252082	0	3,62734188	2,1025638
1,82203159	0	3,17212907	0	3,17212907	3,17838579
2,36439189	0	3,75776803	0	1,98452329	3,71905632
4,1159973	0	2,52275244	0	2,88530958	1,88140728
5,6622258	0	1,94970364	0	3,83035814	4,39179001
2,17081825	0	2,65553924	0	2,76648999	2,62805692



Primary cilia length [µm] SCP-1 N=3, n=3					
Crl	THS [puff/ml]				
	4.10 ⁻⁵	4.10 ⁻⁴	4.10 ⁻³	2.10 ⁻²	4.10 ⁻²
3,14753892	0	3,43239119	0	3,37180107	2,29494238
1,82203159	0	2,62622779	0	0	2,91761033
5,23612771	0	4,04006292	0	0	0
3,65803039	0	2,58334257	0	0	0
1,66917923	0	3,41999776	0	0	0
2,58334257	0	4,08039077	0	0	0
1,8407201	0	3,02773572	0	0	0
3,06157176	0	2,48832624	1,94970364	0	3,35795227
1,57376946	0	4,14098089	2,52275244	0	2,29494238
1,57927765	0	2,65219498	2,78832604	0	1,31412701
2,03586752	0	0	3,44242397	0	2,23778071
2,49521148	0	0	3,15835858	0	2,7090688
0	0	0	1,59540879	0	2,61820146
0	0	0	2,97324395	0	1,498227
0	0	0	1,20904839	0	4,92023976
0	0	0	3,17212907	0	1,78738619
0	1,82203159	0	3,72786641	0	2,42306335
0	1,62216287	0	1,96721182	0	1,70834541
0	2,11475271	0	2,60321141	0	1,41524403
0	2,94708003	0	2,72891624	0	1,70834541
0	3,56281734	0	2,70373593	0	2,10650598
0	2,87626041	0	2,44996561	0	2,00144678
0	3,8726532	0	1,8407201	0	1,91333897
0	1,8639332	0	2,26386737	0	1,58239263
0	2,22944116	0	2,83101454	0	1,21143312
0	3,75540737	0	2,63606385	0	2,4689898
0	3,70937462	0	1,67940873	0	1,41524403
0	2,65553924	0	2,65553924	0	4,37405018
0	1,41245809	0	2,99645705	0	1,59855558
0	2,36439189	1,57927765	4,21514478	2,29868745	4,05867547
0	3,78294834	4,07193176	3,93442365	3,15374714	2,9791084
0	2,67481792	2,76648999	0,99875344	2,35072428	2,15519195
0	3,02773572	2,99055542	3,95409577	1,72845054	0
0	3,01927671	2,99055542	2,04865439	3,79040985	0
0	4,19881692	5,42163579	2,49521148	1,35295752	0
0	3,15835858	3,24432574	2,86426042	3,61537688	0
0	4,90012793	3,35134206	2,70058839	1,78738619	0
1,70498249	2,94708003	4,14727597	2,60321141	2,23778071	0
2,04019538	3,46485019	1,9363266	5,93507808	3,43916126	0
3,21521101	2,91186694	2,43953938	4,14727597	3,1592662	0
3,62734188	5,93507808	1,78386768	2,51921146	3,15374714	0
3,51914523	3,19357168	2,83711289	2,95888331	1,66222185	0



Primary cilia length [µm] SCP-1 N=3, n=3					
	THS [puff/ml]				
Crl	4.10 ⁻⁵	4.10 ⁻⁴	4.10 ⁻³	2.10 ⁻²	4.10 ⁻²
3,8122598	1,70498249	2,73835886	3,02773572	1,532524	
3,71409593	3,34366994	2,37521156	1,3502942	3,53830719	
1,20904839	2,36065419	2,59652289	2,09842485	2,26833263	
1,58458912	1,87770369	1,67940873	3,27875195	4,22345875	
3,9887187	3,9692433	3,34366994	3,9125876	3,15650667	
2,10235928	3,28917817	2,29042473	3,99521049	2,41596742	
4,35953812	3,67219431	2,11475271	4,57514454	2,42306335	
5,31107848	2,5056377	4,5525216	1,97153969	2,26084248	
4,24760377	1,85468731	2,83711289	1,8639332	3,1592662	
1,46635969	3,46248953	3,27875195	1,8267529	1,60407464	
3,47232559	3,08675207	4,16793169	4,1159973	3,12339233	
3,73258772	4,28793161	2,52275244	2,67481792	1,59855558	
1,78386768	1,70498249	2,76648999	4,58084946	2,44435115	
4,14098089	1,57376946	3,17212907	1,20904839	2,47943658	
4,10557108	4,85960337	1,57927765	3,35901419	2,36905543	
4,16596448	3,40976826	3,89488269	2,70373593	1,71327314	
3,65330908	2,86426042	3,07278487	1,70498249	2,05683447	
2,40747383	3,82366962	2,99055542	3,23901427	3,47168428	
3,49947312	3,11724386	2,04019538	1,64321204	2,10650598	
3,65803039	2,70373593	3,75776803	2,80662111	2,03988307	
2,62288353	2,99350623	1,94970364	0	2,99941064	
3,64622712	2,36065419	3,01632589	0	2,49323423	
2,32386733	2,86426042	4,40655449	0	0	
2,77888342	2,29416243	2,80367029	0	0	
3,17212907	2,8882604	3,7760631	0	0	
2,90301449	1,62216287	3,05035866	0	0	
1,31154012	1,67940873	2,15094941	0	0	
3,56753864	2,99055542	3,62734188	0	0	
2,4182935	3,93442365	3,30216177	0	0	
0	3,44989938	2,53278522	0	0	
0	1,65894973	2,23337558	0	0	
0	2,41121153	3,55062062	0	0	
0	0	3,23901427	0	0	
0	0	4,08452191	0	0	
0	0	3,31770274	0	0	
0	0	2,94708003	0	0	
0	0	4,8116034	0	0	
0	0	4,69573463	0	2,6962567	
0	0	3,69324348	0	3,17562627	
0	0	2,73835886	0	1,498227	
0	0	2,04019538	0	3,46931897	
0	0	0	0	3,71905632	



Primary cilia length [µm] SCP-1 N=3, n=3					
Crl	THS [puff/ml]				
	4.10 ⁻⁵	4.10 ⁻⁴	4.10 ⁻³	2.10 ⁻²	4.10 ⁻²
0	0	0	0	2,55138144	
0	0	0	0	3,36820195	
0	0	0	0	2,23383852	
0	0	0	0	1,89520492	
0	0	0	0	1,78738619	
3,95302494	0	0	0	1,66222185	
2,55138144	0	0	0	1,42135442	
3,46931897	0	0	0	2,89395722	
1,95354925	0	0	4,22345875	3,0648509	
3,36563953	0	0	2,93830679	2,07772804	
1,88140728	0	2,35072428	1,64645312	2,42306335	
3,07884565	0	2,52772834	2,17509998	2,17509998	
2,13922611	0	2,18712364	1,48659756	3,71669101	
2,33968616	0	3,19730828	3,65341896	3,95085674	
2,93830679	0	3,02227531	1,66222185	3,29310335	
3,04789951	0	1,78738619	3,53081704	3,79040985	
2,47943658	2,64441698	2,13922611	2,78751826	1,8583455	
1,57687357	2,18712364	1,97542837	2,24546797	2,62805692	
2,32490297	2,9791084	1,86760964	3,57457528	0	
3,29566577	2,36905543	2,66077704	5,17845281	0	
4,35039708	2,8699099	3,2534844	1,78738619	0	
1,46925195	1,58771458	1,31412701	2,95289287	0	
2,42306335	2,11892386	2,84270883	3,02523195	0	
4,86386653	2,99941064	4,20709869	2,55138144	0	
3,12339233	3,53830719	3,53574477	2,07772804	0	
2,12286605	2,7626825	2,50013305	2,7626825	0	
2,36531036	2,13922611	3,25072487	2,90874041	0	
3,0648509	1,62536243	3,62503523	1,39691288	0	
2,42306335	3,15650667	4,19054152	2,61820146	0	
1,95354925	2,41222235	0	2,01011959	0	
2,66077704	1,42135442	0	0	0	
6,7364039	3,13443044	0	0	0	
0	2,01011959	0	0	0	
0	1,41524403	0	0	0	
0	2,24546797	0	0	0	
0	3,53830719	0	0	0	
0	0	0	0	3,13443044	
0	0	0	0	2,32490297	
0	0	0	2,95289287	2,82142104	
0	0	0	2,83048806	2,23778071	
0	0	0	2,18712364	3,06761043	
0	0	3,1592662	2,83048806	4,40558765	



Primary cilia length [µm] SCP-1 N=3, n=3					
	THS [puff/ml]				
Crl	4.10 ⁻⁵	4.10 ⁻⁴	4.10 ⁻³	2.10 ⁻²	4.10 ⁻²
0	0	1,42135442	2,32490297	2,88193356	
2,05269517	0	2,29494238	4,23154023	3,07884565	
4,38587673	0	2,15519195	3,1013161	2,68009375	
1,84435075	0	2,12286605	2,7090688	1,48659756	
2,90282714	0	1,95354925	2,88193356	3,18094821	
3,43916126	0	4,8780584	2,36905543	2,52772834	
4,12628392	0	2,52772834	2,13922611	2,97339223	
1,62536243	0	2,64126323	4,64586376	2,23778071	
2,55138144	0	1,70834541	2,8699099	3,54796554	
2,13922611	0	2,55138144	3,81977912	3,16458815	
4,76156686	0	3,19730828	2,00144678	2,23778071	
1,12273398	0	3,17562627	4,61610027	2,6962567	
3,45670398	0	4,03088307	4,17418145	2,26084248	
2,36531036	1,71327314	2,63140777	1,70834541	2,03988307	
1,76787238	2,47943658	2,74376002	4,04803157	5,07240806	
2,73429877	4,02240737	3,83121145	2,77194663	3,52608642	
2,58173626	4,27825511	1,58239263	4,27825511	1,42135442	
1,32063162	3,70052806	6,60315808	1,94014582	4,10736144	
2,74376002	3,28521898	4,69573239	1,83962013	2,03988307	
2,4689898	2,66077704	3,12339233	2,88193356	0	
2,32490297	1,89520492	2,45479793	3,0928404	0	
2,26833263	1,60407464	3,8107121	2,64441698	0	
2,44435115	1,98843757	0	3,66051489	0	
2,91761033	2,88193356	0	3,71669101	0	
3,02523195	4,81912275	0	0	0	
1,45151212	1,31412701	0	0	0	
3,4164937	2,88193356	0	0	0	
1,60407464	1,97109197	0	0		
2,61820146	2,15519195	0	0		
2,82142104	1,68272121	0	0		
3,64395772	1,46925195	0	0		
0	2,82142104	0	0		
0	2,66077704	0	0		
0	3,83121145	0	0		
0	0	0	0		
0	0	0	2,26084248		
0	0	0	2,68009375		
0	0	0	2,52772834		
0	0	0	2,78751826		
0	0	0	2,17509998		
0	0	0	3,39126373		
0	0	0	1,39691288		



Primary cilia length [μm] SCP-1 N=3, n=3					
	THS [puff/ml]				
Crl	$4 \cdot 10^{-5}$	$4 \cdot 10^{-4}$	$4 \cdot 10^{-3}$	$2 \cdot 10^{-2}$	$4 \cdot 10^{-2}$
		0			
		0			
		0			



Figure 6 Viability 48 h

SCP-1 N=3, n=4 Resazurin							
THS Yellow [puff/ml]							
$4 \cdot 10^{-1}$	$2 \cdot 10^{-1}$	$4 \cdot 10^{-2}$	$2 \cdot 10^{-2}$	$4 \cdot 10^{-3}$	$4 \cdot 10^{-4}$	$4 \cdot 10^{-5}$	crl.
0,1412759	0,6573729	1,180555	1,176961	1,106622	1,059797	1,116788	1,094094
0,1484639	0,5454458	0,9006347	0,951464	0,8389208	0,8006191	0,8044184	1,016669
0,22938	0,4703828	0,7823411	0,7019384	0,6689764	0,7052243	0,7452717	0,8892366
0,1804891	0,5411825	0,79865	0,7295071	0,7236457	0,7372138	0,4991757	1,048411
0,1883043	0,5275059	0,8289339	0,6395237	0,6463621	0,6704589	0,7009599	1,005102
0,2101218	0,5778705	0,7832367	0,7359113	0,6654659	0,7111631	0,8656219	0,9464875
0,1913342	0,5782522	0,7824557	0,6922924	0,7267432	0,7171925	0,9027494	1,068068
0,101512	0,3953104	0,6877444	0,6086099	0,2271494	0,5747275	0,6488593	0,8189532
0,2172576	0,5519877	0,8366902	0,7185569	0,1630232	0,7401597	0,8396464	1,112979
0,1540114	0,4870507	0,3180716	0,7282703	0,6264198	0,6934521	0,8060084	0,9051582
0,1298991	0,5521539	0,8440094	0,7193969	0,7323211	0,7472708	0,769647	0,9936022
0,0621917	0,5404836	0,9623526	0,803983	1,034979	1,004019	1,030156	1,10124

SCP-1 N=3, n≥3 Resazurin							
THS Amber [puff/ml]							
$4 \cdot 10^{-1}$	$2 \cdot 10^{-1}$	$4 \cdot 10^{-2}$	$2 \cdot 10^{-2}$	$4 \cdot 10^{-3}$	$4 \cdot 10^{-4}$	$4 \cdot 10^{-5}$	crl.
0,1620589	0,6759771	1,006312	0,968153	1,103894	0,8988585	0,9823916	1,193123
0,1538954	0,5377679	0,703505	0,643703	0,8170341	0,7175538	0,7543843	0,9797338
0,1333919	0,4398063	0,6448421	0,6362989	0,6142766	0,6630675	0,7150858	0,9415743
0,1582619	0,412848	0,6847101	0,5932034	0,5512471	0,5806735	0,7503975	0,8855692
0,2759307	0,7201691	0,7459157	0,7258421	0,6924587	0,7140597	0,7888995	0,9913814
0,2576026	0,6263466	0,6656212	0,6632211	0,6481658	0,7286786	0,828174	1,004691
0,2859676	0,6573299	0,7203873	0,6931133	0,6680213	0,7319515	0,832756	0,9551616
0,2648029	0,5872903	0,690495	0,6706396	0,7487522	0,6883131	0,7587891	1,048766
0,1754617	0,4367054	0,6877857	0,6861688	0,7018758	0,6813182	0,7824894	0,9478745
0,1643745	0,412221	0,7051096	0,7219715	0,6732337	0,7496896	0,8256836	0,9672772
0,2207347	0,4477926	0,7769458	0,7817965	0,8090526	0,7550023	0,7910359	1,084848



SCP-1 N=3, n=3 Resazurin							
THS Bronce [puff/ml]							
$4 \cdot 10^{-1}$	$2 \cdot 10^{-1}$	$4 \cdot 10^{-2}$	$2 \cdot 10^{-2}$	$4 \cdot 10^{-3}$	$4 \cdot 10^{-4}$	$4 \cdot 10^{-5}$	crl.
0,1837817	0,6928874	1,205943	1,199914	1,112395	1,105951	1,031737	1,155012
0,1696456	0,4985167	0,9063833	0,9618881	1,047744	0,930082	0,8924552	0,9007705
0,1723481	0,5220075	1,106367	0,9932784	1,03631	0,90867	0,7750012	0,944218
0,1149683	0,3585786	1,002069	0,9307844	1,107819	0,9183685	0,7655233	1,07314
0,0933474	0,3290371	0,910876	0,954332	0,9027414	0,9040259	0,8575729	0,9586134
0,1220326	0,3720649	0,8224656	0,8729858	0,7969915	0,7242081	0,8091934	0,9682465
0,2217114	0,4197141	0,8446368	0,8412229	0,7388077	0,6739448	0,7462379	0,8538743
0,2195024	0,5604848	1,013722	0,8980533	0,7755567	0,7886097	0,7054726	1,011312
0,2237195	0,5857874	1,036816	0,8466449	0,827166	0,9335974	0,8317847	1,134813

