



CADMAD

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¹ As specified in Annex I

² i.e. name of the person(s) responsible for the preparation of the document

³ Short name of partner(s) responsible for the deliverable

⁴ The Technical Annex of the project provides a list of deliverables to be submitted, with the following classification level:

Pub - Public.

PP - Restricted to other programme participants (including the Commission Services)

RE - Restricted to a group specified by the consortium (including the Commission Services)

CO - Confidential, only for members of the consortium (including the Commission Services)

⁵ R = Report, P = Prototype, D = Demonstrator, O = Other

⁶ Two digits separated by a dot:

The first digit is 0 for draft, 1 for project approved document, 2 or more for further revisions (e.g. in case of non acceptance by the Commission) requiring explicit approval by the project itself;

The second digit is a number indicating minor changes to the document not requiring an explicit approval by the project.



MINUTES

Paving the Way for Future Emerging DNA-based Technologies: Computer-Aided DNA Processing Utilizing DNA Reuse

CADMAD

The Weizmann Institute of Science, Rehovot, Israel

March 31 & April 1st, 2014 - 36 Month Project Meeting



GENERAL

The 36M CADMAD meeting was held at the Weizmann institute with representatives from all WP's, the project officer and all three reviewers.

Comprehensive summaries from partners were given for all WP's, both for the work done during the 3rd year and for the entire work performed during the 3 years of CADMAD. Overall the CADMAD project has reached its objectives, advancing the state of the art in DNA editing considerably compared to its state at the beginning of the project. These included developments in (1) microfluidics, (2) DNA editing algorithms and (3) DNA editing biochemistry, as evident by several publication in these fields, some already published and some are undergoing the process of publication, all in well known, high impact journals.

The project also opens the way to future collaborations, both commercial and academic in nature between CADMAD associated scientists, primarily in the field of microfluidics, which are now being pursued. Some final experimental work is still due, for example the synthesis of 2 more CADMAD libraries and their experimental validation by CADMD partners. Also, RUB (WP3) have rejected deliverables which are now being addressed by them.

We expect the final 45M meeting to be held in Brussels, possibly with only a small representative, relevant group.

- Final Meeting to be held in Brussels
- Should attend coordinator, WP5 Leader



Internal work package discussions

WP# 2	Developing biochemistry and algorithms for a computer-aided DNA design based on DNA reuse
WP Leader	Ehud Shapiro
Participants	

✓ Discussion - Summary

The major activity that was discussed was the microfluidic primer evaluation project.

New computational analyses of the experimental data from ETH (Whitehead) and Weizmann were discussed and evaluated. It was agreed that no additional experimental results will be generated at this stage and that the current results and analyses will be used to prepare the project for publication.

Partner ETH (Whitehead) is interested in funding further experiments but this will be considered for a different publication. A manuscript of a former test library (intronome) reported in WP2 has been accepted for publication.

✓ Conclusions

Microfluidic primer evaluation will be published using existing results and analyses.

Future cooperation (Weizmann-ETHZ) on primer evaluation is possible.

The WP2 intronome library has been accepted for publication in PLoS Genetics.

Action items

Publication of primer evaluation.

Assessment of new of primer evaluation project.

Person responsible

✓ Weizmann

✓

Deadline

✓ No deadline

✓

WP# 3	Automation of DNA processing based on DNA reuse
WP Leader	John McCaskill
Participants	RUB, WEIZMANN, ALL,

✓ Discussion - Summary

Only minor activities in period 3 for tasks 3.3 and 3.5. 3.1 and 3.2 already finished. So focus of attention at the meeting was on 3.4 parts B and C : separate discussions of these 2 parts.

Recent results were presented in both parts and a strategy for publication agreed.



Reasons for the curious results of Weizmann confirmation of nl scale RUB-produced DNA library discussed.

✓ **Conclusions**

WEIZMANN agreed to complete check of DNA test library sent (in customs) by RUB

Publication of C with RUB and WEIZMANN in preparation

Publication of B with ALL and WEIZMANN under revision

Action items

Person responsible

Deadline

Further analysis of RUB nl-library plates.

✓ Weizmann

✓ April?

Special Notes: The results of the review for WP3 need to be digested and acted upon.

WP# 4	Multi-layer system integration and the development of faults detection, isolation and correction methodologies
WP Leader	Ehud Shapiro
Participants	

✓ **Discussion - Summary**

The major activities that were discussed were the various computational tools for evaluating robot liquid handling and other robot operations. The current level of system integration was also discussed. Finally, the completed and Ongoing DNA library editing projects for CADMAD partners were discussed.

✓ **Conclusions**

3 libraries were successfully edited and delivered (2 more are to be delivered).

1 library is in production

1 library will be in production soon.

Robotic QC system will be published.

Action items

Person responsible

Deadline

Publication of robot QC

✓ Weizmann

✓ No deadline

Complete DNA library production

✓ Weizmann

✓ October

✓

✓

WP# 5	End users' applications: Directing system development and potency validation
WP Leader	UKB
Participants	WEIZMANN, UNOTT, UNEW, ETHZ, FMI, UH

✓ **Main Objectives**



- (1) to focus and direct the development of the CADMAD platform to current and future DNA programming requirements,
- (2) to validate the produced libraries and
- (3) to compare the CADMAD libraries against libraries made by existing technologies.

In the third and fourth year of the project the main objectives of this work package are the validation of the produced libraries and the comparison of CADMAD libraries against libraries made by existing technologies. There was one deliverable in the third year of the project, namely: "Operational prototype system constituting the complete CAD and CAM of a DNA library." Furthermore, work has been started to achieve the two remaining deliverables at M45: D5.1: "Critical comparison of results obtained using CADMAD libraries and traditional DNA libraries" and D5.2: "Report on biological results of using the CADMAD libraries".

✓ **Discussion - Summary**

The current status of CADMAD library production was presented:

Name of partner	Short title of library	Specification of library?	Oligos sent to WEIZ?	Library in construction?	Library delivered?	Sequences validated?	Biological function tested?
ETHZ	Combinatorial synthetic operon library	yes	yes	completed	yes	in progress	in progress
FMI	Sequence replacement library	yes	yes	completed	yes	yes	in progress
UNEW	DNA origami	yes	no	no	no	no	no
UH	Glycosylation screening	yes	yes	yes	no	no	no
UKB	Oct4 expression library	yes	no	no	no	no	no
UNOTT	Pseudomonas aeruginosa azurin	yes	yes	completed	yes	yes	in progress
UNOTT	Pseudomonas aeruginosa PqsR	yes	no	no	no	no	no

WEIZ has already delivered libraries of FMI and UNOTT, which have been sequence validated. After cloning UNOTT's library showed an error rate of approximately 1 in 2000 bp, whereas FMI could detect 92% of designed sequences after next generation sequencing and retrieve 85% of fragments. Both error rates are comparable with these of commercially synthesized fragments. Both partners are presently working on D5.2: "Report on biological results of using the CADMAD libraries".

ETHZ's library has also been delivered by WEIZ and sequence validation is in progress. Libraries of UH and UKB will be delivered shortly to the individual partners.

To discuss first biological results and experiences using CADMAD libraries an internal WP5-meeting should take place in May/June 2014 as preparation for the final meeting.



✓ **Conclusions**

Monday March 31, 2014 - Noon
36 Month Project Meeting (Day I)
Location: Ziskind Building

<i>Time</i>	<i>Title</i>	<i>Responsible person</i>	<i>Location</i>
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Each partner will receive the designed library during the course of the CADMAD project.

Partners are presently validating delivered libraries and generating first biological results. Comparison with conventionally synthesized library subsets is in progress.

Action items

Person responsible

Deadline

Downstream processing of delivered CADMAD libraries	✓ WP5 members	✓ October 2014
Comparison of CADMAD libraries with traditionally synthesized library subsets	✓ WP5 members	✓ October 2014

Assigned internal deliverables

From		To		Deliverable description	Purpose	Due Date
WP5	ALL	WP5	ALL	Downstream processing of library subsets	Evaluation of libraries made by conventional DNA-synthesis	October 2014
WP5	ALL	WP5	ALL	Downstream processing of CADMAD libraries	Evaluation of CADMAD libraries	October 2014

Foreseen Internal Meetings

Participants	Purpose	Date	Place
WP5	Workshop/webconference on CADMAD libraries, conventionally synthesized library subsets and their biological applications.	May/June 2014	UKB



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CADMAD

Third Review Meeting

April 2, 2014

At the Weizmann Institute of Science

On April 1, 2014

Reviewers' preparatory meeting

18:00 – 20:30

Hotel Leonardo Boutique, Rehovot

Wednesday April 2, 2014 CADMAD 3rd Review Meeting Location : Koshland Meeting Room, Belfer Building		
Time	Title	Responsible person
9:00	Opening of the Meeting Welcome remarks Prof. Zvi Livneh Dean of the Faculty of Biochemistry	Prof. Ehud Shapiro - WEIZMANN
9:10	Introduction of the attendees	Prof. Ehud Shapiro
9:15 – 9:45	Status of CADMAD Project Coordinator General Overview on the project	Prof. Ehud Shapiro
<u>Work Package Presentations</u> <i>Review of work done over the third year – 20 min. presentation – 10 min discussion/questions</i> <i>For WP3 30 minutes presentation and 15 minutes questions/discussions</i> <ul style="list-style-type: none"> • planned objectives (generally and for period under review) • achieved objectives (in terms of deliverables and milestones) • deviations from original plans <u>in terms of technical work as well as use of resources.</u> • future work • reviewers questions 		
9:45– 10:15	WP1 Developing textual and graphical tools for computer-aided DNA library specification	UNOTT/UNEW – Prof. Natalio Krasnogor
10:15 – 10:45	WP2 Developing biochemistry and algorithms for a computer-aided DNA design based on DNA reuse	WEIZMANN – Dr. Tuval Ben-Yehzekel
10:45 – 11:00	Break	
11:00 – 11:45	WP3 Automation of DNA processing based on DNA reuse	RUB – Dr. Uwe Tangen/Prof.



		John McCaskill
11:45 – 12:05	WP3 Automation of DNA processing based on DNA reuse	WEIZMANN – ALL Dr. Tuval Ben-Yehezkel
12:05 – 12:35	WP4 Multi-layer system integration and the development of faults detection, isolation and correction methodologies	WEIZMANN – Dr. Tuval Ben-Yehezkel
12:15 – 12:45	WP5 End users' applications: Directing system development and potency validation	UKB – Dr. Sandra Meyer
12:45 – 13:15	Free questions	Moderator: Dr. Tuval Ben-Yehezkel
13:15– 13:45	Lunch break	Near the Koshland Meeting Room
14:00 – 15:00	Demonstration of robotic and microfluidic DNA editing systems in Ehud Shapiro's laboratory	Dr. Tuval Ben-Yehezkel
15:00 – 15:15	WP6 Dissemination and Exploitation	OSM - Dr. Prina Dan
15:15 – 15:30	WP7 Management and Technical Coordination Review project administrative , financial and reporting procedures	OSM – Dr. Prina Dan
15:30	Group photo outside the building	
15:35– 15:50	Break	
15:35– 17:05	Reviewers private meeting	Project Officer and Reviewers In Room 225 in Belfer Building
17:05 – 17:20	Presentation of the Review Results and Discussion	Dr. Teresa de Martino
17:20	Closing the meeting	Prof. Ehud Shapiro
18:30	Pick-up transportation for dinner in Tel Aviv from San Martin Guesthouse first, then from Leonardo and back to Rehovot a 22:00.	Daniella to order transportation
19:15	Dinner at Lehem Basar Restaurant Hangar 14, Namal Tel Aviv (Tel Aviv Harbor)	



List of Participants

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