

Site Visit Review

Laboratory of Method Development

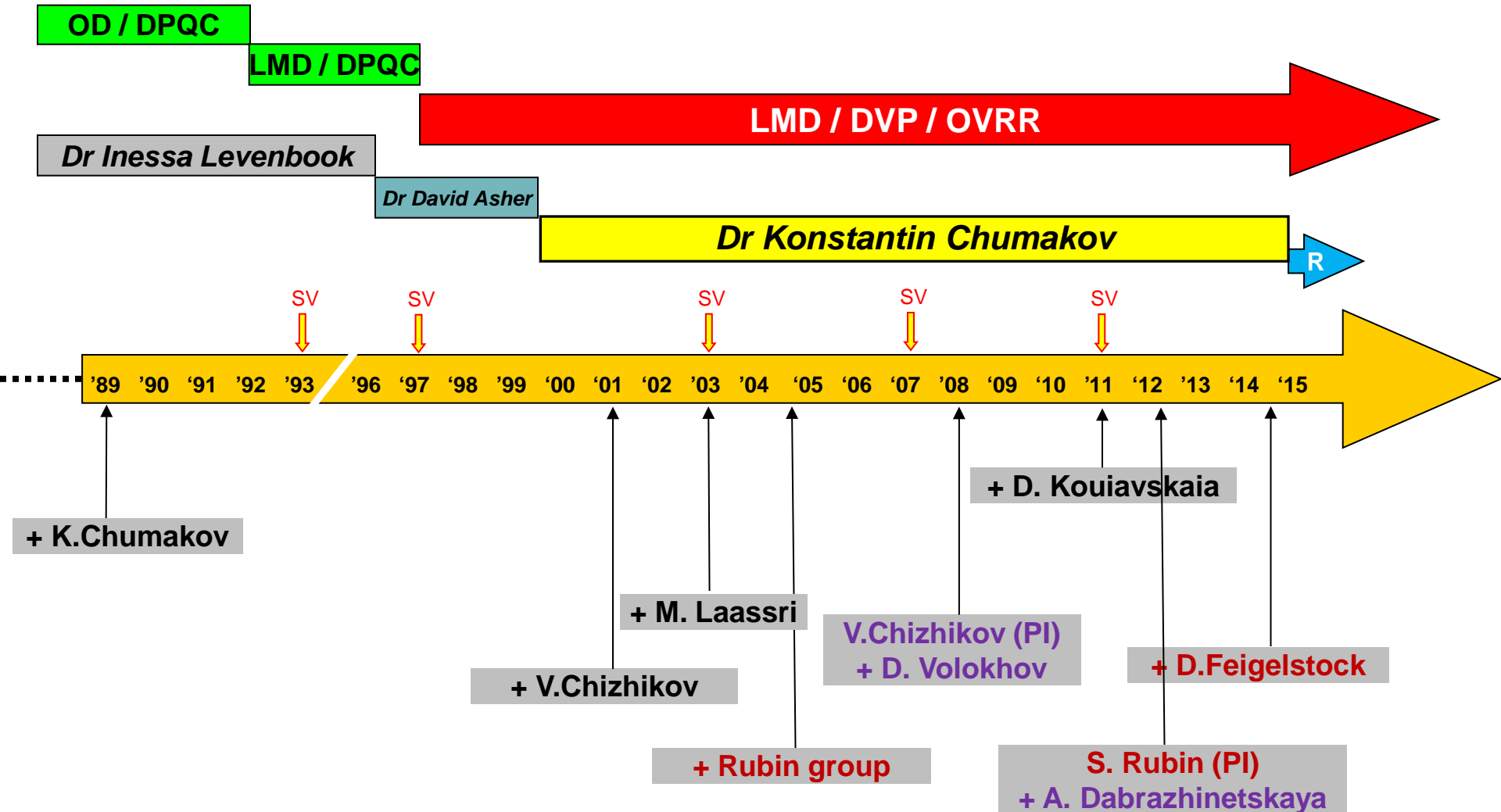
FDA/CBER/OVRR/DVP

Steven A. Rubin, Acting Chief, LMD

LMD Mission Statement

To conduct research leading to creation of new concepts, methods, and reagents for quality control and evaluation of new and existing viral vaccines

History of LMD



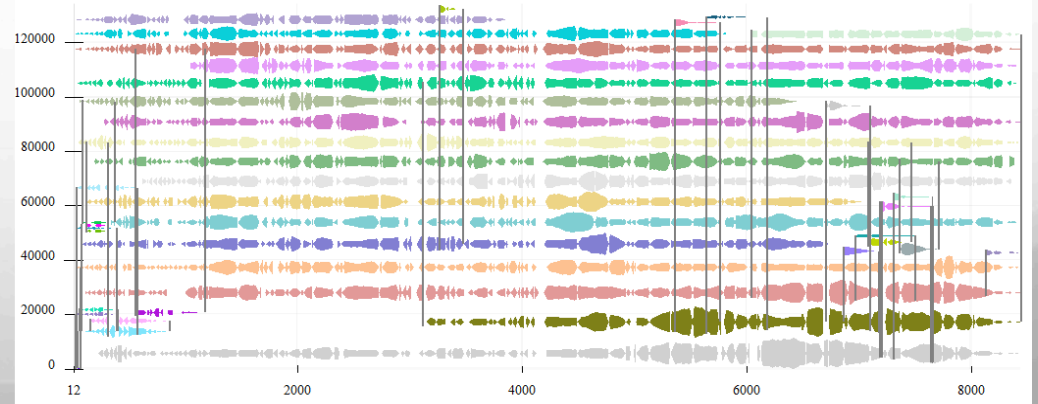
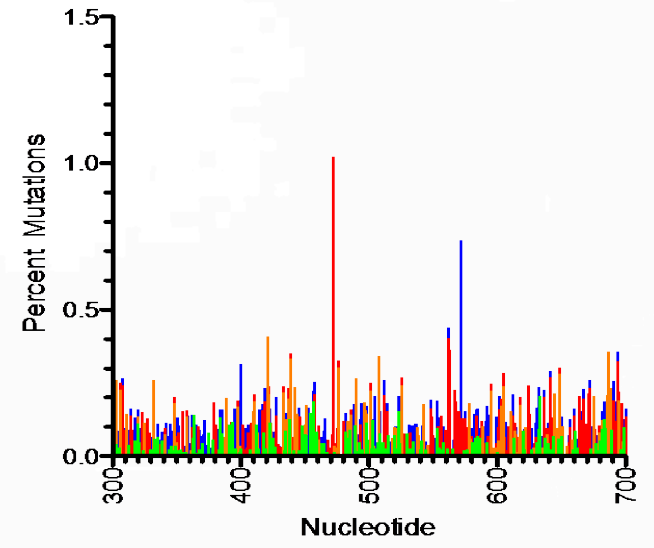
LMD Research Programs

- **Chumakov**: Evaluation of safety and potency of viral vaccines based on analysis of molecular consistency (Z01 BK 08013-10)
 - *Genetic and antigenic consistency of vaccines*

Konstantin Chumakov, PhD, DSci	Principal Investigator
Olga Miroshnichenko, MS	Biologist
Majid Laassri, PhD	Biologist
Monica Parker, BS	Biologist
Diana Kouivaskaia, MD, PhD	Staff Fellow
Eugenia Dragunsky, MD, PhD	Volunteer
Tatiana Zagorodnyaya, BS	ORISE Fellow
Svetlana Petrovskaya, PhD	ORISE Fellow

Projects-Chumakov's Group

- Tools for monitoring genetic stability of viral vaccines
- Design of genetically stable attenuated poliovirus vaccines
- Metagenomic-based environmental surveillance of pathogenic viruses



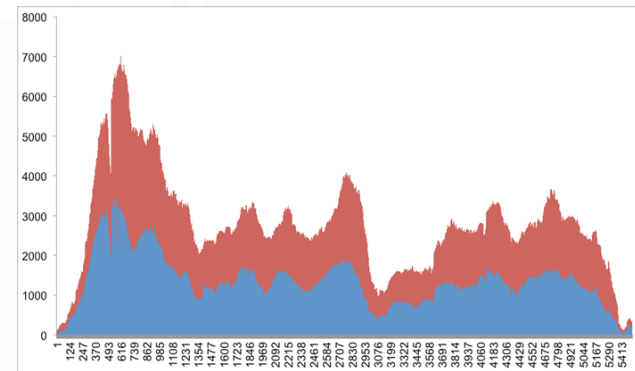
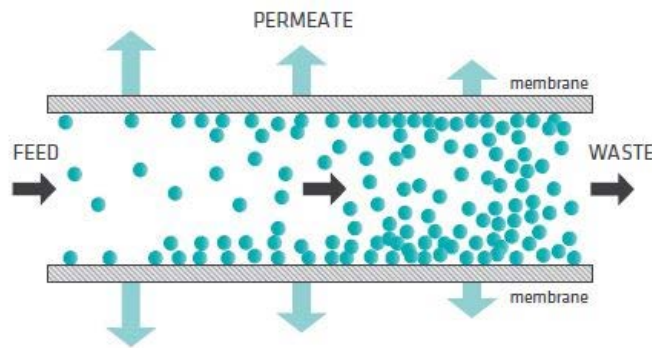
LMD Research Programs

- **Chizhikov**: New ways to improve testing of vaccines for purity and safety (Z01 BK 08014-10)
 - *Adventitious agents*

Vladimir Chizhikov, PhD	Principal Investigator
Dmitriy Volokhov, DVM, PhD	Biologist
Alena Dabrazhynetskaya, PhD	Staff Fellow
Qin Shuyun	ORISE Fellow
Vyacheslav Furtak, PhD	ORISE Fellow

Projects- Chizhikov's Group

- Tangential flow filtration and deep sequencing for detection of adventitious agents during vaccine manufacture



- Mycoplasma reference strains- nucleic acid test-based testing
- Development of an in vitro alternative to the LD50-based rabies vaccine potency test

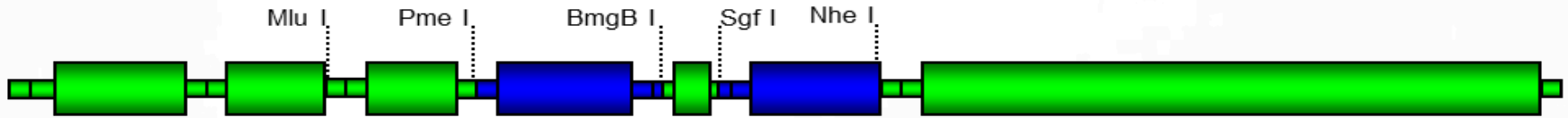
LMD Research Programs

- **Rubin**: Determining the Safety and Efficacy of Vaccines to Protect Against Viruses that Infect the Central Nervous System (Z01 BK 08015-10 LMD)
 - *Virulence and Attenuation*

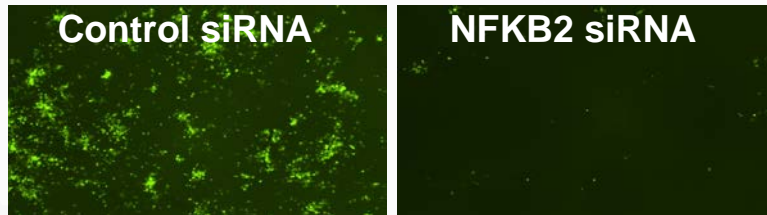
Steven Rubin, PhD	Principal Investigator
Tahir Malik, PhD	Biologist
Christian Sauder, PhD	Biologist
Dino Feigelstock, PhD.	Biologist
Laurie Ngo, MS	Biologist
Hanson Chen, PhD	ORISE Fellow

Projects- Rubin's Group

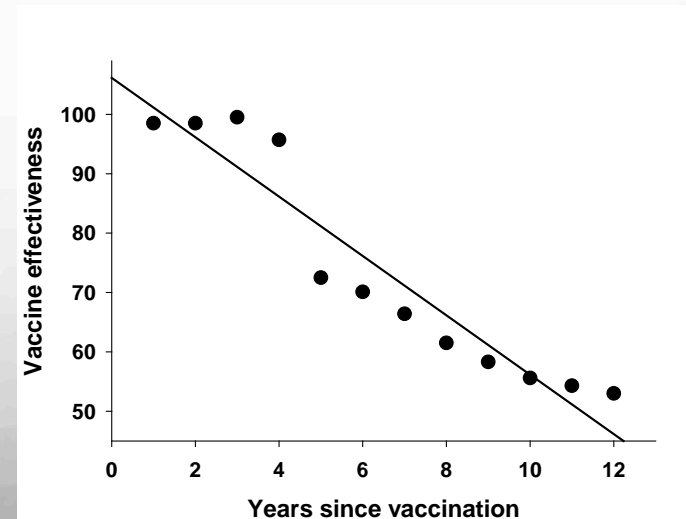
- Identification of genetic markers of virus attenuation



- Identification of cellular targets for rational vaccine design



- Investigations of mumps outbreaks in the US



LMD Publications during Site Visit review period

2011 (>July)	2012	2013	2014	2015 (<July)	Total
12	12	9	13	6	52

Scope of Regulatory Responsibilities

- Licensed Vaccines (BLAs and BLA supplements)
 - Poliovirus vaccines and combinations
 - Mumps, Measles, Rubella, Varicella vaccines
 - Rotavirus
 - Rabies
 - Influenza vaccines
- Investigational Vaccines (pre-IND and IND)
- Lot release (IPV, MMR vaccines)
- Facility inspections
- Guidance documents

LMD regulatory review activity during Site Visit review period

Master Files	IND's			BLAs		Totals
	<i>pre</i>	<i>Original</i>	<i>Amend.</i>	<i>Original</i>	<i>Suppl.</i>	
11	22	14	338	4	211	601

Guidance Documents- Since last SV

- **(2011-Final): Guidance for Industry: Process Validation: General Principles and Practices**
(<http://www.fda.gov/downloads/Drugs/Guidances/UCM070336.pdf>)
- **(2014- Final): Guidance for Industry: Product Development Under the Animal Rule**
(<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM399217.pdf>)
- **(2015- Draft): Guidance for Industry: Established Conditions: Reportable CMC changes for Approved Drug and Biologic Products (DRAFT)**
- **(2015- Draft): Staff Manual Guide: Inter-center coordination of regulatory activities for genetically engineered animals and their expression products**
- **(2015- Draft): World Health Organization Points to Consider: Clinical development of Ebola vaccines (DRAFT)**

International Activities

- Advising WHO on vaccines issues
 - WHO Drafting Group: Recommendations for manufacturing and control of Polio vaccines
 - WHO Polio Research Committee
 - WHO Polio anti-Viral initiative steering group
- International workshops collaborative studies
 - Polio virus vaccines, anti-virals, and assay standards/specifications
 - Rabies virus vaccines and potency testing
 - Ebola virus immunological and diagnostic test standards
 - Mycoplasma test methods and reference reagents
- Others
 - Global Virus Network
 - Task Force for Global Health
 - Bill and Melinda Gates Foundation consortium on poliovirus vaccines