

University of Groningen

## Novel Approaches for Developing Small Molecules to Target Histone Deacetylases

Cao, Fangyuan

DOI:  
[10.33612/diss.157448844](https://doi.org/10.33612/diss.157448844)

**IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.**

*Document Version*  
Publisher's PDF, also known as Version of record

*Publication date:*  
2021

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*  
Cao, F. (2021). *Novel Approaches for Developing Small Molecules to Target Histone Deacetylases*. University of Groningen. <https://doi.org/10.33612/diss.157448844>

### Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

### Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

*Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.*

# APPENDICES

**A**

---

**Acknowledgement**

**Publication**

**About the author**



## Acknowledgement

The final words of my thesis are a trip down the memory lane of my life in Groningen for the last four years. Groningen is a lovely city, where I am grateful to meet and work with so many delightful and brilliant people. Without their guidance and support, I would not be able to enjoy my PhD journey in Netherlands. Therefore, I would like to take this opportunity to express my deep gratitude to all those people that helped me during this journey.

First of all, I would like to express my most sincere gratitude to my supervisor **Prof. Frank J. Dekker**. Dear **Frank**, it is my honor to be one of your PhD students. Thank you for choosing me to join and work in such an awesome group to expend my knowledge in medicinal chemistry field. All my PhD achievements could not be obtained without your guidance and support. You always know how to direct and encourage me to plan the project and solve the problem. I will never forget the scientific research thinking that I learned from you. Apart from research, you are knowledgeable, patient and humorous, when talking about European culture and history. Thank you for inviting me to visit the Dutch pasture and attend your daughter's baptism. These were my first time to go deep into the Dutch life, which indeed made me like the Netherlands more. Also, I kept all the Christmas cards that you sent to me every year, which have warmed my winter days in Groningen. Thank you for everything, and I wish you, your beautiful wife and your lovely kids a happy life.

I also would like to thank my second supervisor, **Prof. Gerrit J. Poelarends**. Dear **Gerrit**, Thank you for your helpful suggestions and remarks during my PhD period. You are productive and approachable, and your door is always open for me. I appreciate your advices for my career development, and I wish you and your family a happy life. Many thanks also go to **Prof Wim J. Quax** and **Prof. Hidde J. Haisma** for your kind remarks in group meeting for my PhD projects. Thank you for making the department of Chemical and Pharmaceutical Biology such a wonderful scientific platform. I also would like to thank **Prof. Finn K. Hansen** and **Prof. Wiktor Szymanski** for the guidance and advices in the corporative work, which have expanded my knowledge in HDAC related field.

In the meantime, I would like to thank the members of my assessment committee: **Prof. A.S.S. Dömling**, **Prof. P.H. h. Elsinga** and **Prof. R.J. Pieters** for taking time to read and evaluate my thesis.

## Acknowledgement

Thanks also go to **Petra**, who is our bio-lab captain. You are generous and always ready to help the others. Thank you for helping me with my research project and sharing your excellent biological technology with me. Dear **Pieter**, it is a lot of fun to talk with you. Thank you for making our chem-lab in good order. I also would like to thank **Ronald**. Thank you for introducing Discovery Studio software to me, which helps me a lot in my project.

I would like to thank my officemates in 3215-0108A, **Martijn, Hao, Zhangping, Angelina**. We have spent happy and harmony time together in the office. I am lucky to meet each of you. **Martijn**, we have cooperated perfectly in HDAC-related field, and I wish you every success in your business. **Hao**, you are a humorous person that makes the office full of joy. I wish you and **Yu Tian** a sweet and happy life. **Zhangping**, you are brilliant and diligent. Thanks for your sincere friendship, assistance and support. I wish you and **Shanshan** all the bests. **Angelina**, it is nice to talk with you, and I wish your PhD study goes smoothly. **Hannah**, many thanks for sharing your experience and giving many hugs to me in my first year in Groningen. I hope everything goes well with you in Edinburgh. **Siwei**, my paranymp, we have spent a lot of time travelling together. You are such a kind and sweet person who loves life so much. I wish all the bests for your future. **Deng**, I am quite impressed by your superior scientific skills, as well as your cooking skills. I wish you a happy life with **Yi Guo, Olivia** and **Bin**, many thanks for sharing your biological experience with me. I enjoyed coffee time with you so much. Furthermore, I also would like to mention some other lovely group members in our department. My sincere thanks to **Rita, Robert, Haigen, Alex, Lieuwe, Saif, Saravanan, Jielin, Baojie, Chao, Andreas, Marie, Michele, Eleonora, Laura, Fabiola, Yizhou, Yafeng, Siqi, Fengzhi, Xinyu, Abel, Magda, Ingy, Putri, Joko, Jan** for all your kind help. I enjoyed all our group trips and parties, and I wish you all the bests. For the new members in the department, **Kristina, Sandy, Chunlong, Micheal, Ting, Bo, Nika, Feyza, Sara**, I wish you a great time in the department.

There are also some people from other department that I would like to thank **Andre** and **Robin** from Department for Drug Design for assistance. Many thanks also go to **Eduard** and **Catharina** from the group of Pharmacokinetics, Toxicology and Targeting for the kind help.

I also would like to thank my friends in Groningen for their support and accompany, which makes my life more colorful. **Qian, Beibei** and **Jiajia**, thank you for being my very first friends in Groningen. I am lucky to meet such trustworthy friends that mitigated my homesick for the

first few months. **Xiu**, you are a thoughtful and assertive girl. Many thanks for inviting me as your paranymp. I wish you a bright future. Thanks also go to **Yi Yu, Lulu, Shuai Feng, Yafeng, Jian Gao, Shun Fang, Weiteng, Mengfan**. I will never forget the cheerful days that we spent in Stationsplein 9. I also would like to thank **Jingyao, Xiaoxiang, Lin Zhou, Qian Wang, Zefeng, Bidong, Chao Wang, Daozheng** for the pleasant lunch time in Eriba. Many thanks also go to **Xiaoyan Long, Keni, Yana, Bingquan, Xiaoxuan, Cheng Wang, Yuequ, Yanmei, Dan Li, Mei Li, Chongnan, Yuhan** for the wonderful time we spent together.

Special thanks to dear **Guangcai**. You are my serendipity, the one that makes all my moments memorable. Thanks for accompanying me to get through the most difficult time. Thanks for always being optimistic when I am upset and worried. Thanks for your favor and love.

The last but not the least, I would like to thank my family.

亲爱的爸爸妈妈，感谢你们的养育之恩，在我成长的每一步都给予我坚定的支持和无私的爱。无论何时何地，我们仨个永远在一起。我还要感谢姥姥，小姨，姨夫，舅舅，舅妈，大姑和二伯对我的关心和支持。

December, 2020

Fangyuan

## Publication

[1] **Cao F.**, de Weerd S., Chen D, Zwinderman M.R.H., Ettema P.E., Dekker F.J., Induced protein degradation of histone deacetylases 3 (HDAC3) by proteolysis targeting chimera (PROTAC). *Eur J Med Chem.* 2020 Sep.

[2] **Cao F.**, Zwinderman M.R.H., van Merkerk R., Ettema P.E., Quax W.J., Dekker F.J., Inhibitory selectivity among class I HDACs has a major impact on inflammatory gene expression in macrophages. *Eur J Med Chem.* 2019 Sep 1;177:457-466. doi: 10.1016/j.ejmech.2019.05.038.

[3] **Cao F.**, Zwinderman M.R.H., Dekker F.J., The Process and Strategy for Developing Selective Histone Deacetylase 3 Inhibitors. *Molecules.* 2018 Mar 2;23(3). pii: E551. doi: 10.3390/molecules23030551.

[4] **Cao F.**, Zhou X., Su J., Yang X., Mu F., Shen J., Sun W., Chemical Structure Characteristics and Bioactivity of Small Molecule FAK Inhibitors. *Anticancer Agents Med Chem.* 2016;16(8):934-941. doi: 10.2174/18715206166661511 16122355.

[5] Liu B., Chen S., Rose A., Chen D., **Cao F.**, Zwinderman M., Kiemel D., Aïssi M., Dekker F. J., Haisma H.J., Inhibition of histone deacetylase 1 (HDAC1) and HDAC2 enhances CRISPR/Cas9 genome editing. *Nucleic Acids Res.* 2020 Jan 24;48(2):517-532. doi: 10.1093/nar/gkz1136.

[6] Krieger V., Hamacher A., **Cao F.**, Stenzel K., Gertzen C. G. W., Schäker-Hübner L., Kurz T., Gohlke H., Dekker F. J., Kassack M. U. & Hansen F. K., Synthesis of peptoid-based class I selective histone deacetylase inhibitors with chemosensitizing properties. *J Med Chem.* 2019 Dec 26;62(24):11260-11279. doi: 10.1021/acs.jmedchem.9b01489.

[7] Zwinderman M., **Cao F.** & Dekker F., Acetylation and Methylation in Asthma, COPD, and Lung Cancer. Oct-2019, *Chemical Epigenetics.* Mai, A. (ed.). Berlin: Springer Nature, p. 1-25

## Patent

[1] Li S., Xiao J., Xu L., Cao R., **Cao F.**, Wang H., Zhong W., Zheng Z., Xie Y. Zhou X. Wang X., A kind of 4-oxos-4,5-thiazolines analog derivative, Preparation Method And The Use. 2017-06-09. CHINA. Publication of CN106810509A.

## About the author

Fangyuan Cao was born on 24th of April 1990 in Changchun, China. She obtained her bachelor degree in Pharmacy from Jilin University in 2012. She continued her master study in Jilin University under the supervision of Prof. Xiaohong Yang, and she obtained her master degree in medicinal chemistry in 2016. During her master period, she involved in a joint-master program from lab of Prof. Song Li in Beijing Institute of Pharmacology & Toxicology, to develop broad-spectrum antiviral molecules as clathrin inhibitors. After the completion of her master degree, she started her doctoral program in October 2016 in the department of Chemical and Pharmaceutical Biology, University of Groningen. Under the supervision of Prof. Frank J. Dekker, she applied novel strategies to develop histone deacetylases (HDACs) antagonists for treatment of inflammation and cancer. The results of her PhD research are presented in this thesis.