

# 生物工学研究センターセミナー

## くすりのシリコンバレーTOYAMA 講演会 (グレーガー教授連続講演会 1)

Strategies for the Production of Generic Pharmaceuticals:

Novel Retrosyntheses & Flow Processes

ジェネリック医薬品製造の戦略：新しい逆合成解析とフロープロセス

日時：平成31年2月19日(火)

15時00分～16時30分

場所：富山県立大学 生物工学科研究センター K115 共同会議室

来聴歓迎 (参加自由)

講師：Harald Gröger 氏

(ドイツ：ビーレフェルト大学 教授)



### 講演要旨：

The development of competitive production processes for generic pharmaceuticals represents a challenging task. One approach to achieve such processes is the design of alternative retrosynthetic routes with minimized number of steps, low solvent consumption and avoidance of toxic substrates, reagents and catalysts. In this presentation an overview about our recent work in this field, which has been done in part with industrial partners, is given. For example, novel syntheses of key intermediates or active pharmaceutical ingredients (APIs) of Rosuvastatin, Cefotaxime, Tamsulosin, and Vildagliptin will be presented.

Furthermore, flow processes for pharmaceutical purpose gain increasing importance, and their development meets the guidelines of the regulatory agencies U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA). Advantages are that the desired product quality can be more easily ensured and that numbering up of flow modules enables an elegant increase of the production scale without facing scale up concerns. Examples in this field will be also given related to chemo- and biocatalytic reactions.

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# 生物工学研究センターセミナー

## くすりのシリコンバレーTOYAMA 講演会 (グレーガー教授連続講演会 2)

Process development of biotransformations for technical applications in the chemical and pharmaceutical industry

化学・製薬産業での工業化を目指したバイオ物質変換による生産プロセス開発

日時：平成31年2月20日(水)

15時00分～16時30分

場所：富山県立大学 生物工学科研究センター K115 共同会議室

来聴歓迎 (参加自由)

講師：Harald Gröger 氏

(ドイツ：ビーレフェルト大学 教授)



### 講演要旨：

A major focus of biocatalysis is on the development of synthetic processes fulfilling the criteria of high efficiency, sustainability and scalability as well as the application of such biotransformations as key steps for the production of chemicals from various industrial value chains.

In this research area of bioprocess development Harald Gröger and his teams (in industry until 2006, at the University of Erlangen-Nürnberg from 2006 to 2011 and at Bielefeld University since 2011) developed a range of biocatalytic technology platforms. Within these interdisciplinary projects jointly with collaboration partners several processes running on industrial scale have been realized. Examples of the developed biotransformations are the asymmetric ketone reduction and  $\alpha$ -keto acid reductive amination technologies based on the use of recombinant whole cell catalysts. Both types of processes run at high substrate loading of typically  $>100$  g/L and give the desired products with  $>99\%$  ee. Recently, new biocatalytic processes have been developed using ene reductases (for C=C-reduction), aldoxime dehydratases (for nitrile synthesis) and imine reductases (for C=N reduction).

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# 生物工学研究センターセミナー

## くすりのシリコンバレーTOYAMA 講演会 (グレーガー教授連続講演会 3)

Combination of the two "worlds" chemo- and biocatalysis towards multi-step one-pot processes

—複数反応を単一反応器で行う—

化学触媒と生体触媒の二つの“世界”の組み合わせ

日 時： 平成 31 年 2 月 22 日 (金)

15 時 00 分～16 時 30 分

場 所： 富山県立大学 生物工学科研究センター K115 共同会議室

来聴歓迎 (参加自由)

講 師： **Harald Gröger** 氏

(ドイツ：ビーレフェルト大学 教授)



### 講演要旨：

Multi-step one-pot processes represent an attractive synthetic concept for the improvement of overall process efficiency by decreasing the required number of work up and purification steps. By avoiding such time-, capacity- and solvent-intensive process steps, multi-step one-pot syntheses contribute to a significantly improved process economy as well as to more sustainable synthetic routes. A key criterion for multi-step one-pot processes is the compatibility of the individual reaction steps with each other. Accordingly, most of today's known multi-step one-pot processes are based on either chemocatalytic multi-step reactions or “pure” biotechnological processes such as, e.g., fermentation. In contrast, successful combinations of chemo- and biocatalytic reactions, in particular in aqueous reaction media, are much less widely known.

In this contribution strategies for the combination of chemo- and biocatalysts towards the development of multi-step one-pot processes in aqueous reaction media are presented. Examples will be given demonstrating that enzymatic reactions can be combined with metal-catalyzed as well as organocatalyzed reactions.

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