YVES P. AUBERSON
EFMC PRESIDENT
NOVARTIS INSTITUTES FOR BIOMEDICAL RESEARCH
BASEL (SWITZERLAND)

THE CHANGING LANDSCAPE OF MEDICINAL CHEMISTRY

The European Federation for Medicinal Chemistry (EFMC) represents the medicinal chemistry and chemical biology community of 24 countries, and over 7,500 medicinal chemists. EFMC aims to advance the science of medicinal chemistry and chemical biology by promoting cooperation, training and networking, by rewarding scientific excellence, and by facilitating communication.

Medicinal Chemistry is the design, synthesis and optimization of pharmacologically active molecules for use as tools in cell biology, as drug candidates or as imaging agent. It is a dynamic, constantly evolving discipline, as illustrated by the trends of the last decades, such as parallel synthesis and chemical libraries, rules and indexes for drug-likeness, or, more recently, new modalities, chemical biology and chemically optimized biologics. Predicting forthcoming changes in medicinal chemistry is obviously a challenge, but a few directions can be highlighted with confidence. Most visibly, an upcoming transformation will result from the power of digitalization. While the influence of true artificial intelligence remains to be seen, our ability to compile and analyze vast amounts of data will have a clear impact. Medicinal chemists will soon benefit from these advances through the use of recommenders, programs designed to provide suggestions for synthesis integrating yield prediction, starting material availability, and a diversity of synthetic methodologies. As we draw new molecules on the screen, these programs will compute physicochemical properties, suggest potential biological activities, provide information on known structural analogues, and make proposals for initial structural modifications. The potential for support from high-volume data set compilations is vast and many applications will emerge, becoming part of the medicinal chemist toolbox.

Another area that will certainly develop in the near future is automation and miniaturization. Synthetic chemists often still work like thirty years ago, mixing compounds in glass round-bottom flasks and stirring solutions mechanically before manual workup and purification. This process can be automatized, for instance using microtiter plates or flow chemi-

stry, and robotics. Such devices are already used in specialized laboratories, and will become more broadly accessible. They will be followed by semi-independent optimization systems to automatize the exploration of simple structure-activity relationships. While a strong medicinal chemist will remain indispensable for the optimization of more complex molecules and sophisticated parameters, the basic variations around simple substituents and well-described, robust chemistries, hopefully will not take so much of his or her time any more.

A number of new technologies developed rapidly over the last few years, with the potential to revolutionize chemistry and life sciences. Progress in analytics already influence the practice of medicinal chemistry, enabling sensitive target engagement assays and detailed studies of drug metabolism. Biocatalysis, to explore novel chemical space, is also becoming more prominent, as well as surfactant and flow chemistry, to enable sustainable and continuous drug manufacturing. The recent extension of electron diffraction techniques to low-molecular weight compounds will open new horizons for medicinal chemists, hopefully providing structural information faster and to a lower cost. Ultimately, we should however not forget that progresses in synthetic organic chemistry remains critical, as more robust and versatile synthetic methodologies will be required to further expand the scope of research in medicinal chemistry. This is particularly obvious in areas where medicinal chemistry diversifies, supporting the synthesis and optimization of new modalities, DNA-encoded libraries or novel chemical entities.

Overall, the potential for development in medicinal chemistry is enormous. Machine learning and artificial intelligence, outsourcing tactics, new technologies, progress in therapeutic biologics and gene or cell therapies will all support and expand its scope. Medicinal chemists must grab these opportunities and lead the change, taking advantage of developments in related fields to shape the future of the discipline. We must not hesitate to outsource routine chemistry, a low value-added component of medicinal chemistry which is a hindrance to the exploration of the more sophisticated problems at which medicinal chemists excel. We must focus on the design of new molecules with complex profiles and specific properties, to ultimately discover new drug candidates and tools to explore cellular processes. We must also embrace digitalization, which brings immense opportunities. Increasingly sophisticated applications will give us real-time predictions and recommendations to help design better molecules. This is going to be a relief for medicinal chemists in all areas where massive data collection and analysis plays a critical role. It will help expand the scope of medicinal chemistry, taking advantage of the options offered by new targets and synthetically enhanced biologics. Even though formulation and targeted delivery will likely be a challenge for many new modalities, they will help address problems that are beyond the current scope of low-molecular weight compounds.

Under these conditions, and with the obvious need to select better targets for therapeutic intervention, the interaction between medicinal chemists, chemical biologists and clinical scientists is bound to grow stronger. There is strength in unity, as well as in scientific diversity, and medicinal chemistry has a bright future ahead. By using the most modern technologies to provide new tools to study biology and treat diseases, it can change the world, for the better.