The Drug Discovery Game is an engaging, interactive demonstration of the methods used in modern medicinal chemistry. Students (playing the role of medicinal chemists) are given seed capital and challenged to invent a small molecule pharmaceutical starting from a Velcro-equipped scaffold and Velcro-equipped molecular fragments. The teacher (playing the role of a biologist assigning compounds) provides feedback after each student’s educated guess that guides the student toward the solution. The Drug Discovery Game, intriguing at both college and high school levels, launches discussions of such topics as the methods of modern drug invention, the cost of pharmaceuticals, organic synthesis, molecular structure and design, and structure-activity relationships.

**Goals**

- Provides an enticing springboard from which the process of discovery and FDA approval of new pharmaceuticals can be discussed.
- Specifically teaches the trial and error development of structure-activity relationships (SAR) that encompasses every medicinal chemist’s workflow.
- Emphasizes the vastness of medicinal chemical space (with estimates as high as 10^{10} possibilities).\(^1\)
- Introduces the concept that drug discovery research requires a significant investment. Currently, it is estimated that the cost to invent and develop a new pharmaceutical treatment is $2.56 billion.\(^2\)

**Abstract**

- The rules of the game are similar to the popular game "Mastermind".\(^3\)
- Students are told that they have just started a drug discovery company attempting to find a treatment for a particular disease. They are also given $700 in "seed capital" to play.
- The student plays the role of the medicinal chemist. The teacher plays the role of the biologist conducting an assay.
- The chemist/student assembles a molecule by attaching "molecular fragments" to the Velcro attachment points on the "scaffold". The student presents the assembled molecule to the biologist/teacher for assay along with $100 in play money. (Each guess costs the student $100.)
- The biologist/teacher tells the chemist/student how many of the "molecular fragments" in the molecule are correct and how many are in the right Velcro space on the scaffold. (The biologist/teacher does not tell the chemist which pieces are correct or which pieces are in the correct place.)
- The student uses the information gained from each assay attempt to logically determine the correct combination of pieces.
- Pieces can be used more than once.
- Each student is allowed to complete the puzzle before the demonstration continues.

**Rules of the Game**

- After all students complete the Allegra puzzle, a short discussion of how much time and money is spent on preclinical screening or by messiking natural agonists or antagonists. Opponents of these fees follows a trial and error path similar to the game being played.

**Example of Gameplay using Allegra**

![Scaffold Diagram](Image)

- The table below presents an example of the interaction between the student/chemist and the teacher/biologist. A medicinal chemist develops structure-activity relationships through a similar process of trial and error.
- The demonstration concludes with a discussion of the three stages of drug discovery. Not all new pharmaceuticals must successfully pass through all three stages. It pointed out that in 11 000 candidates that enter human trials make it to the market.\(^3\)
- Students are asked to review the amount of play money they have at the end of the game and to consider the cumulative cost of each step along the path of developing a new pharmaceutical. It is explained that a current estimate of the cost to bring a new pharmaceutical to market is $2.56 billion.

**Flow of the Demonstration**

- Conclusion

- A fast-paced, interactive game has been developed as a springboard to discuss modern medicinal chemistry.
- The challenge of synthesizing a properly optimized pharmaceutical is emphasized through a comparison of the vast number (10^7) of possible drug-like molecules with the small number of possible molecules (625) for solving the simplistic puzzles in the game.
- The use play money emphasizes the costs of research and opens a discussion of the increasing price of pharmaceuticals.\(^4\)
- The presentation of drug discovery as a puzzle to be solved will hopefully entice students to take up the challenge and bring fresh innovation to medicinal chemistry.

**Further Examples**

- Some other drugs employed in the game are outlined in the table below. Further examples have included Albuterol, Singular, and Zeta.

**Further Examples**

- A typical lesson using this game is provided below. The demonstration takes approximately 45-60 minutes depending on the depth of the discussion that occurs between games.

**Set-up**

- Molecular fragments and scaffold are drawn on ChemDraw; printed on sturdy card stock, and cut out.
- Course Velcro is attached to the underside of the fragments.
- Soft Velcro is attached to the attachment points on the face of the molecular scaffold.

**Summary**

- The game is a good tool to supplement other material and to introduce the vastness of chemical space, the many obstacles to discovering a new drug, and the cost to bring a medicinal chemical to market.