

Organic Pharmaceutical Chemistry IV

Fifth Stage

Lecture 15

ENCODING COMBINATORIAL LIBRARIES

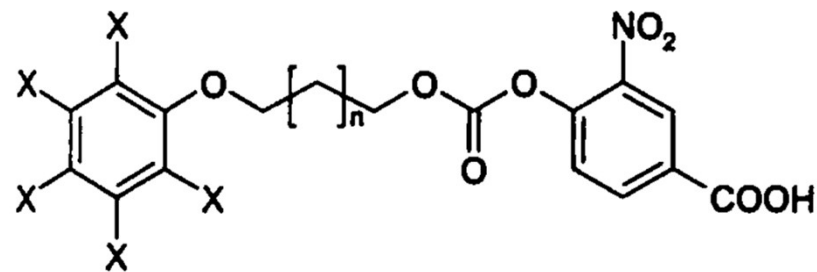
- Used to determine which structure is responsible for activity
- Physical labels
 - Good for small libraries of one-bead one-compound resin

ENCODING COMBINATORIAL LIBRARIES

- For solid phase library attach a chemical tag to the resin beads
- One of the earliest methods is to use DNA as a tag
 - For decoding the DNA is amplified by PCR

ENCODING COMBINATORIAL LIBRARIES

- Polyhalogenated aromatic compounds
- Isotopically labeled peptides and dyes



ENCODING COMBINATORIAL LIBRARIES

- Radiofrequency encoding
- Laser optical encoding
- Semiconductor particle

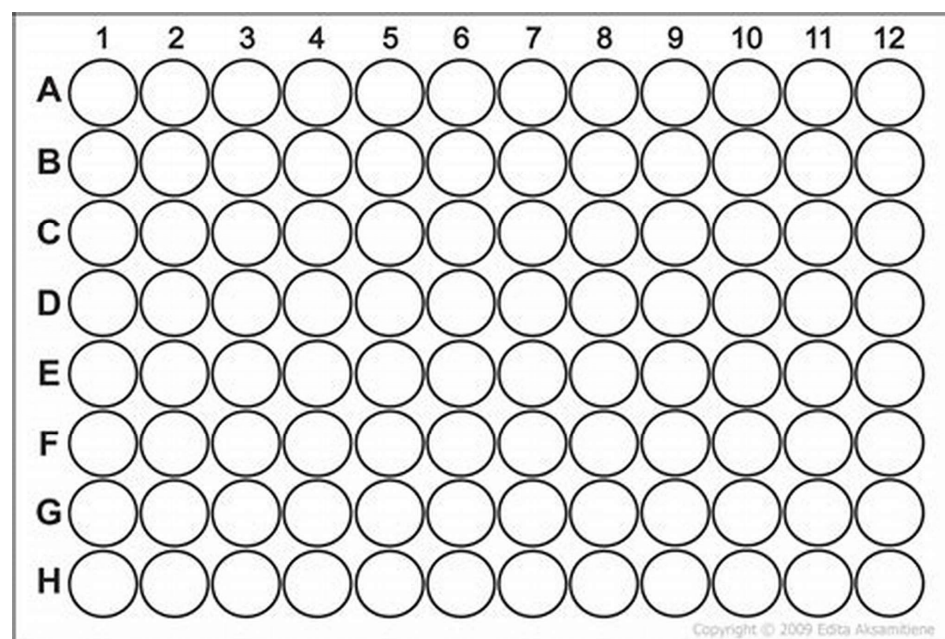
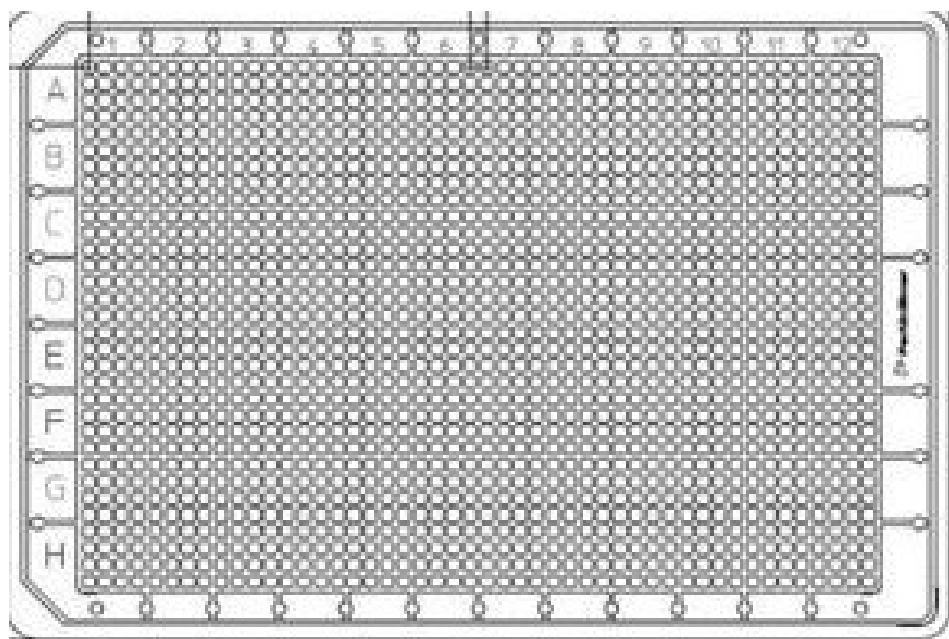
HIGH-THROUGHPUT SCREENING (HTS)

1. Enzymes
2. Organelles
3. Cells
4. Tissues
5. Organs
6. Animal

HIGH-THROUGHPUT SCREENING (HTS)

- a) Target identification
- b) Reagent preparation
- c) Compound management
- d) Assay development
- e) High-throughput library screening

HIGH-THROUGHPUT SCREENING (HTS)



HIGH-THROUGHPUT SCREENING (HTS)

‡ Targets

- i. Cell membrane receptors (about 45% of the total)
- ii. Enzymes (28%)
- iii. Hormones (11%)
- iv. Unknowns (7%)
- v. Ion channels (5%)
- vi. Nuclear receptors (2%)
- vii. DNA (2%)

HIGH-THROUGHPUT SCREENING (HTS)

‡ Libraries

‡ Pooling

‡ Assay

- ❖ Solubility of compounds

- ❖ Concentration

HIGH-THROUGHPUT SCREENING (HTS)

‡ Detection

- 1) Nonradiometric
 - a. Absorbance
 - b. Fluorescence
 - c. Luminescence
- 2) Radiometric
 - I. Filtration
 - II. Scintillation proximity assay (SPA).