

1.3 Définition d'une cible :

Une cible est le point d'impact moléculaire responsable de l'effet thérapeutique du médicament. C'est une macromolécule de l'organisme, protéine ou glycoprotéine, capable de :

- × Se lier avec une substance,
- × Modifier la protéine et entraîner une réponse cellulaire.

Remarque : Si la macromolécule ne fait que fixer la substance sans entraîner de réponse cellulaire, il s'agit d'un site de liaison.

Quelles sont les familles de cibles thérapeutiques ?

Les grandes familles de cibles sont :

→ **Les récepteurs** : visés par environ 50 % des médicaments :

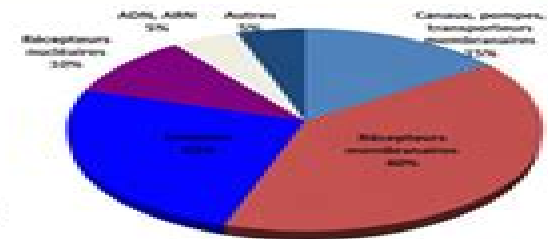
- Les récepteurs membranaires :
 - Les récepteurs couplés aux protéines G (25 %).
 - Les récepteurs enzymes ou canaux (15 %).
- Les récepteurs nucléaires (10 %)

→ **Les pompes et canaux ioniques** : visées par environ 15 % des PA.

→ **Les enzymes** : visées par environ 25 % des molécules actives.

Remarques :

- Ces quatre familles correspondent à près de 90 % des médicaments.
- 5% des molécules se lient à des cibles diverses.
- 5% dont la cible reste inconnue (dont celle du paracétamol).



2 Les Récepteurs :

Définition : structures protéiques dont la fonction est de lier un ligand spécifique, ligand naturel (endogène → médiateur) ou un médicament (exogène), et de transmettre une information par conversion de cette interaction en un effet (transduction), c'est-à-dire en une modification du fonctionnement cellulaire.

Principes fondamentaux des récepteurs :

- Une même cellule contient plusieurs types de récepteurs.
- Les liaisons ligand récepteur sont réversibles et saturables.
- Les récepteurs sont stéréospécifiques ex : l'énantiomère S se fixe mais pas le R.

2.1 Quel est le mode d'action des médicaments sur les récepteurs ?

Les médicaments peuvent agir sur les récepteurs de trois manières :

→ **Agonistes** : reproduit l'effet du ligand naturel (médiateur).

× **Agoniste entier** → effet identique à celui du médiateur.

× **Agoniste partiel** → effet inférieur à celui du médiateur.

→ **Antagonistes** : empêche l'effet du ligand naturel.

× **Antagoniste compétitif** → le médicament se lie au même site que le médiateur.

× **Antagoniste non compétitif** → se lie à un autre site du récepteur (site allostérique) et entraîne une diminution de l'affinité du récepteur pour son médiateur.

× **Antagoniste négatif** ou agonistes inverses → réponse opposée à celle de l'agoniste.

× **Antagoniste neutre** → s'oppose à la liaison du médiateur à son récepteur mais sans entraîner de réponse cellulaire → Diminution de l'effet du médiateur correspondant.

→ **Modulateurs** des sites allostériques (différents du site récepteur) pour les récepteurs canaux (activation, limitation).

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RJ Alexander



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