

# Drug resistance

Gulshan Kumar  
School of Fisheries

# Introduction

- Drug resistance is the reduction in effectiveness of a medication such as an antimicrobial or an antineoplastic in treating a disease or condition.
- The term is used in the context of resistance that pathogens or cancers have "acquired", that is, resistance has evolved. Antimicrobial resistance and antineoplastic resistance challenge clinical care and drive research. When an organism is resistant to more than one drug, it is said to be multidrug-resistant.

- The development of antibiotic resistance in particular stems from the drugs targeting only specific bacterial molecules (almost always proteins). Because the drug is so specific, any mutation in these molecules will interfere with or negate its destructive effect, resulting in antibiotic resistance.
- Furthermore, there is mounting concern over the abuse of antibiotics in the farming of livestock, which in the European Union alone accounts for three times the volume dispensed to humans – leading to development of super-resistant bacteria.

# Mechanisms

- The four main mechanisms by which microorganisms exhibit resistance to antimicrobials are:
- Drug inactivation or modification: e.g., enzymatic deactivation of Penicillin G in some penicillin-resistant bacteria through the production of  $\beta$ -lactamases.
- Alteration of target site: e.g., alteration of PBP — the binding target site of penicillins — in MRSA and other penicillin-resistant bacteria.

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- Alteration of metabolic pathway: e.g., some sulfonamide-resistant bacteria do not require para-aminobenzoic acid (PABA), an important precursor for the synthesis of folic acid and nucleic acids in bacteria inhibited by sulfonamides. Instead, like mammalian cells, they turn to utilizing preformed folic acid.
- Reduced drug accumulation: by decreasing drug permeability and/or increasing active efflux (pumping out) of the drugs across the cell surface