

# Distinguishing between drug-susceptible and resistant *Neisseria gonorrhoeae* from urine samples by image recognition AI.

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## Background

Gonorrhea is a major public health concern because it causes complications that can seriously affect maternal and newborn health, including infertility and neonatal eye infections leading to blindness. Antimicrobial resistance (AMR) of the causative pathogen, *Neisseria gonorrhoeae* (*Ng*), emerged shortly after antimicrobial agents started to be used. Gonorrhea superbugs can be a major challenge inducing prolonged complications of gonococcal infection and increasing the number of patients with complications. Here, we demonstrated whether resistant *Ng* can be morphologically distinguished from susceptible *Ng* using our artificial intelligence (AI)-assisted image recognition of Gram-stained specimens, which are inexpensive and can be diagnosed in the clinical field.

## Method

Gram-stained images of a drug-susceptible strain of *Ng* (①DS-*Ng* group) and two drug-resistant strains of *Ng* (②DR-*Ng* group) dissolved in female human urine (Lee Biosolutions, Inc.) samples were prepared. There are several drug resistance mechanisms such as  $\beta$  lactamase and penicillinase in antimicrobial resistant *Ng*, and the mutation of PBP (penicillin binding protein) could alter the structure of the bacterial walls. Therefore, we selected PBP mutant strains for this POC study. In addition, the images of bacterial strains of *Neisseria flavescens* and *Moraxella catarrhalis* were prepared as commensal Gram-negative coccus bacteria (③other GNC group). The cell images were acquired using a microscope (Nikon ECLIPSE Ci-L plus) at 1000x magnification and a smartphone (iPhone X) and the number of images for the bacterial distinguishing AI construction was about 600 for three groups. Of these, 60% of the images were used as training data and 20% as validation data. As a final test, about 20% of the images were used to check the accuracy.

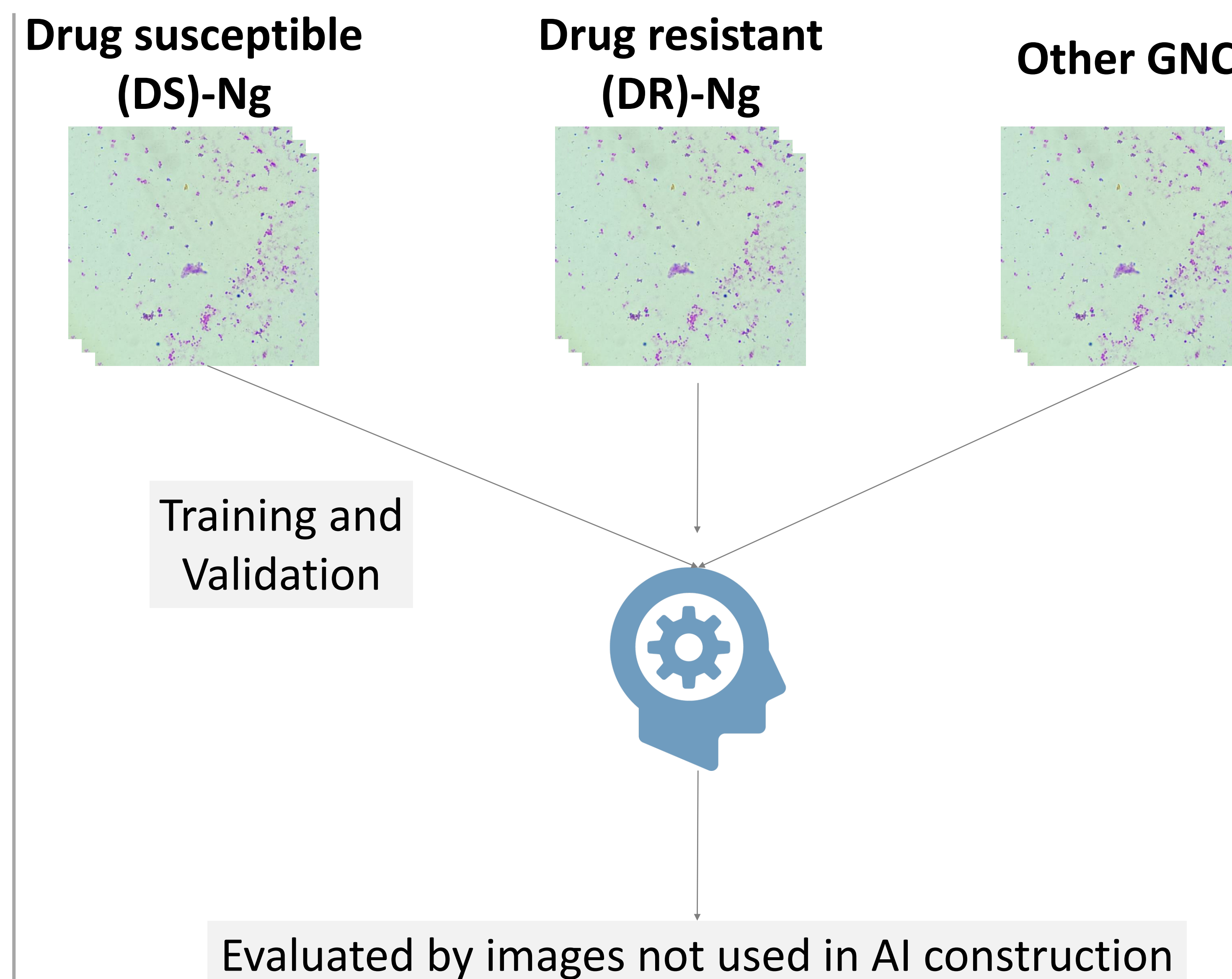


Figure1. Scheme of AI construction and evaluation

## Results

Table1. Confusion matrix of the test results of classifying susceptible *Ng* (DS-*Ng*), resistant *Ng* (DR-*Ng*) and other GNC(Gram-negative cocci).

True label	DR	42	0	4
	DS	0	20	0
	Other	4	0	69
		DR	DS	Other
		Prediction label		

Table2. The test results of the preliminary AI-model classifying susceptible *Ng* (DS-*Ng*), resistant *Ng* (DR-*Ng*) and other GNC.:

Support: number of images included in the test data  
Precision = TP / (TP + FP)  
Sensitivity = TP / (TP + FN)  
Specificity = TN / (TN + FP)  
Accuracy = (TP + TN) / (TP + FN + TN + FN)  
where TP = True Positive, TN = True Negative, FP = False Positive, FN = False Negative

	Precision	Sensitivity	F1-score	Specificity	Support
DR- <i>Ng</i>	91.3%	91.3%	91.3%	95.7%	46
DS- <i>Ng</i>	100%	100%	100%	100%	20
Other GNC	94.5%	94.5%	94.5%	93.9%	73
Accuracy	-	-	-	94.2%	139
Macro Avg.	95.3%	95.3%	95.3%	96.6%	139

## Conclusion

Our preliminary AI model was able to distinguish drug-resistant *Ng* from drug-susceptible *Ng* on Gram-stained specimens, demonstrating the potential for low-cost point-of-care diagnosis of *Ng*. However, We only used a small number of strains for AI model construction so we should collect more *Ng* strains to improve the accuracy and prevent deep learning overfitting. Even though the primary limitation is the rarity of Gram stain for gonorrhea diagnosis, we have developed an automated Gram-stain machine and plan to integrate this AI into our AI-assisted microorganism estimation smartphone app. Such an easy diagnosis will promote the Gram-stain-based proper use of antimicrobial agents, which can help to prevent the spread of drug-resistant *Ng*.