

Supplementary Information

Repurposing FDA-approved antimalarial drugs: Mefloquine as a promising multi-targeted therapeutic for non-small cell lung cancer

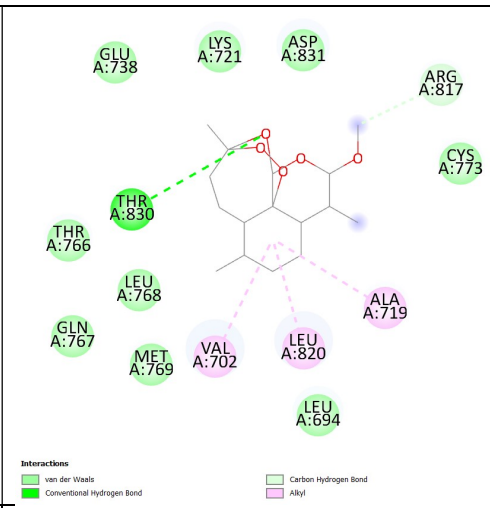
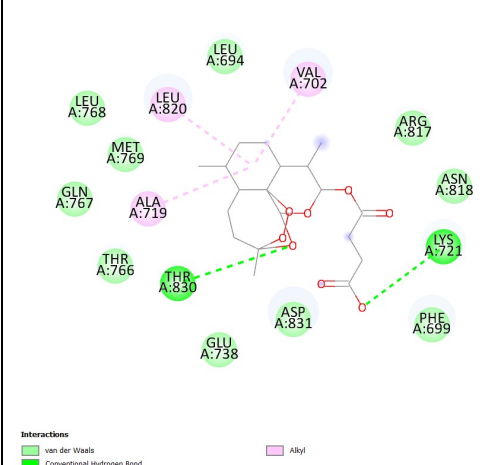
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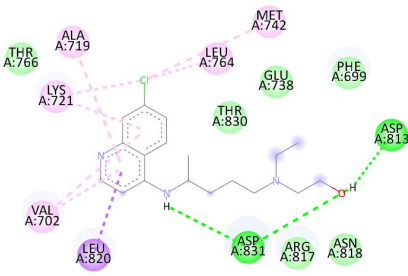
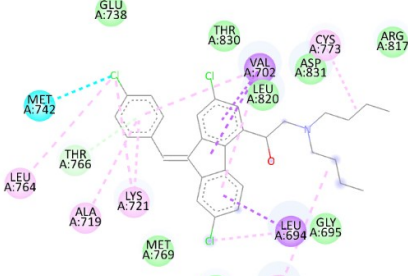
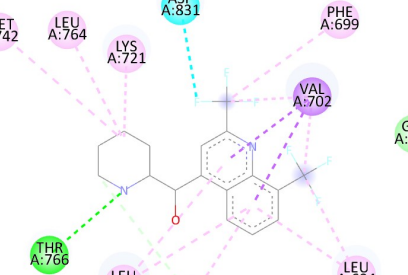
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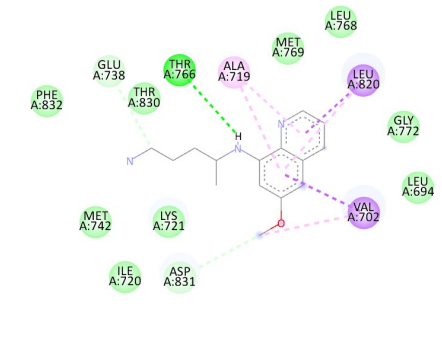
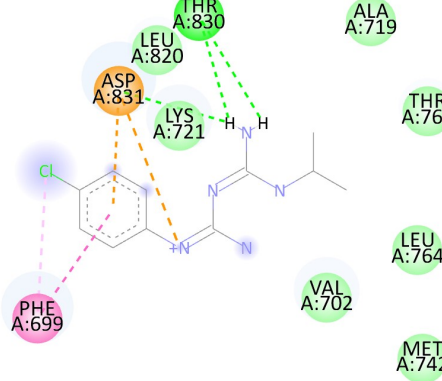
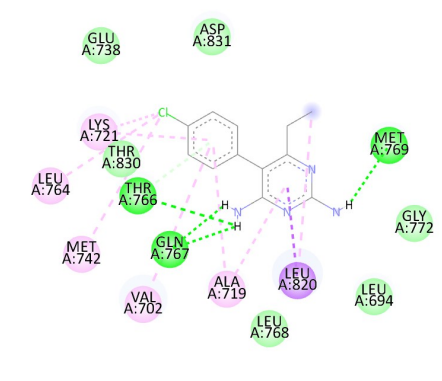
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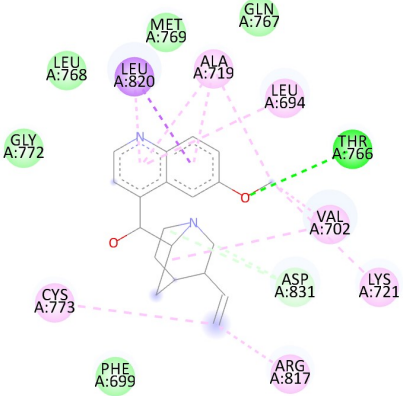
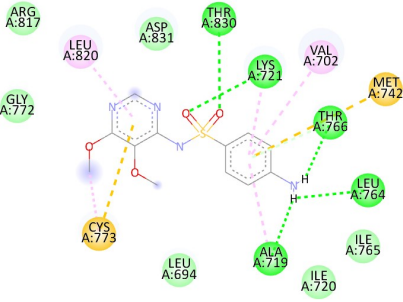
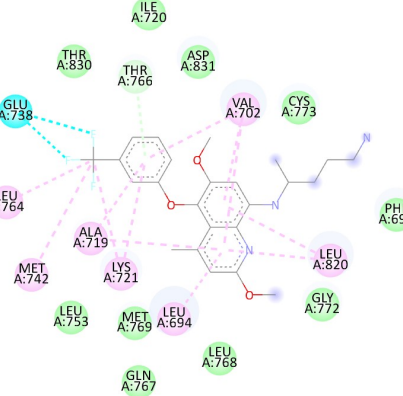
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Table S-1			
Sr.No.	Drug	Amino acid interaction	Diagram
EGFR			
1	Artemether	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Thr830, Arg817 • Hydrophobic interactions: Val702, Leu820, Ala719 	
2	Artesunate	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Thr830, Lys721 • Hydrophobic interactions: Val702, Leu820, Ala719 	

3	Atovaquone	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Thr830, Asp831, Thr766 • Hydrophobic interactions: Val702, Leu820, Ala719, Leu694, Leu764, Lys721 • Electrostatic interactions: Lys721 	<p>Interactions</p> <ul style="list-style-type: none"> von der Waals Konventioneller Wasserstoff-Bond Pi-Cation Pi-Donor Wasserstoff-Bond Alkyl Pi-Alkyl
4	Chloroquine	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Thr766, Arg817 • Hydrophobic interactions: Phe699, Val702 • Electrostatic interactions: Asp831 • Miscellaneous interactions: Cys773 	<p>Interactions</p> <ul style="list-style-type: none"> von der Waals Carbon-Wasserstoff-Bond Pi-Anion Pi-Sulfur Pi-Pi gestapelt Pi-Alkyl
5	Doxycycline	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Asp813, Glu738, Lys721 	<p>Interactions</p> <ul style="list-style-type: none"> von der Waals Conventional Hydrogen Bond

6	Hydroxychloroquine	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Asp831, Asp813 • Hydrophobic interactions: Leu820, Lys721, Ala719, Leu764, Met742, Val702 	 <p>Interactions</p> <ul style="list-style-type: none"> von der Waals Konventioneller Hydrogen Bond Pi-Sigma Allyl Pi-Allyl
7	Lumefantrine	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Thr766 • Hydrophobic interactions: Phe699, Val702, Leu694, Lys721, Leu764, Ala719, Cys773 • Halogen interactions: Met742 	 <p>Interactions</p> <ul style="list-style-type: none"> von der Waals Halogen (Cl, Br, I) Pi-Donor Hydrogen Bond Pi-Sigma Allyl Pi-Allyl
8	Mefloquine	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Thr766, Ala719 • Hydrophobic interactions: Phe699, Val702, Leu694, Leu820, Leu764, Lys721, Met742 • Halogen interactions: Asp831 	 <p>Interactions</p> <ul style="list-style-type: none"> von der Waals Konventioneller Hydrogen Bond Carbon Hydrogen Bond Halogen (Fluorine) Pi-Sigma Allyl Pi-Allyl

9	Primaquine	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Thr766, Glu738, Asp831 • Hydrophobic interactions: Val702, leu820, Ala719 	 <p>Interactions</p> <ul style="list-style-type: none"> von der Waals Conventional Hydrogen Bond Carbon Hydrogen Bond Pi-Sigma Alkyl Pi-Alkyl
10	Proguanil	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Thr830, Asp831 • Hydrophobic interactions: Phe699 • Electrostatic interactions: Asp831 	 <p>Interactions</p> <ul style="list-style-type: none"> von der Waals Attractive Charge Conventional Hydrogen Bond Pi-Anion Pi-Pi Stacked Pi-Alkyl
11	Pyrimethamine	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Thr766, Gln767, Met769 • Hydrophobic interactions: Leu820, Val702, Ala719, Lys721, Leu764, met742 	 <p>Interactions</p> <ul style="list-style-type: none"> von der Waals Conventional Hydrogen Bond Pi-Donor Hydrogen Bond Pi-Sigma Alkyl Pi-Alkyl

12	Quinine	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Thr766, Asp831 • Hydrophobic interactions: Leu820, Ala719, Leu694, Val702, Lys721, Arg817, Cys773 	 <p>Interactions</p> <ul style="list-style-type: none"> von der Waals Conventional Hydrogen Bond Carbon Hydrogen Bond Pi-Sigma Alkyl Pi-Alkyl
13	Sulfadoxine	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Thr766, Thr830, Lys721, Leu764, Ala719 • Hydrophobic interactions: Val702, Leu820, Cys773 • Miscellaneous interactions: Met742, Cys773 	 <p>Interactions</p> <ul style="list-style-type: none"> von der Waals Conventional Hydrogen Bond Pi-Donor Hydrogen Bond Pi-Sulfur Alkyl Pi-Alkyl
14	Tafenoquine	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Thr766 • Hydrophobic interactions: Val702, Leu820, Leu694, Lys721, Ala719, Met742, Leu764 • Halogen interaction: Glu738 	 <p>Interactions</p> <ul style="list-style-type: none"> von der Waals Halogen (Chlorine) Pi-Donor Hydrogen Bond Alkyl Pi-Alkyl
MET			

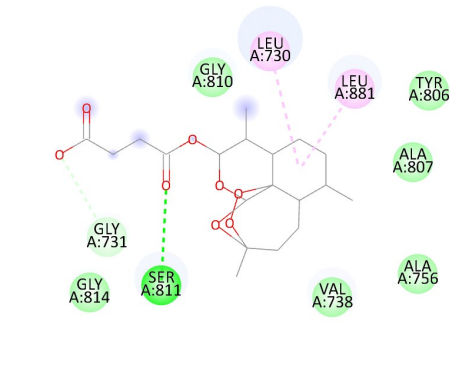
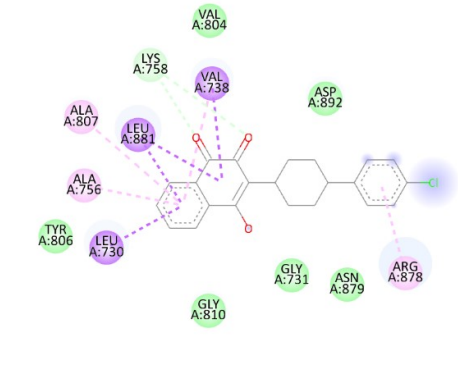
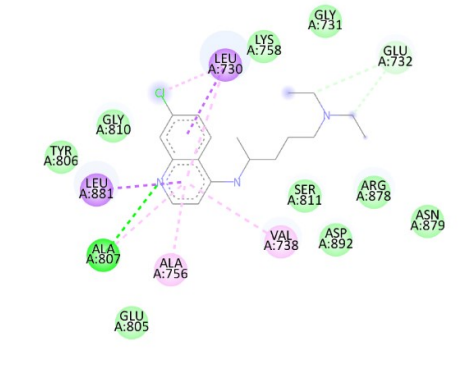
1	Artemether	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Gly1085, Pro1158 • Hydrophobic interactions: Tyr1230, Met1211, Ala1221 	<p>Interactions</p> <ul style="list-style-type: none"> van der Waals Conventional Hydrogen Bond Carbon Hydrogen Bond Pi-Sigma Allyl
2	Artesunate	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Met1160, Tyr1159, Gly1085 • Hydrophobic interactions: Tyr1230, Met1211, Ala1221 	<p>Interactions</p> <ul style="list-style-type: none"> van der Waals Conventional Hydrogen Bond Carbon Hydrogen Bond Pi-Sigma Allyl
3	Atovaquone	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Tyr1230, Asn1209 • Hydrophobic interactions: Tyr1230, Ala1226, Ala1221, Met1211 • Miscellaneous interactions: Met1211 	<p>Interactions</p> <ul style="list-style-type: none"> van der Waals Conventional Hydrogen Bond Pi-Donor Hydrogen Bond Pi-Sulfur Pi-Pi Stacked Pi-Allyl

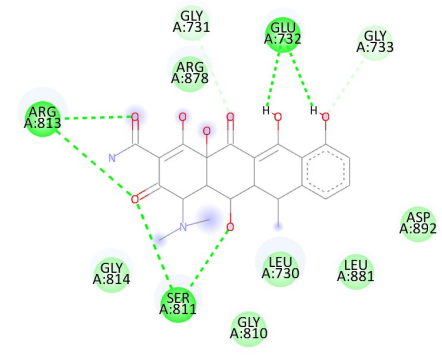
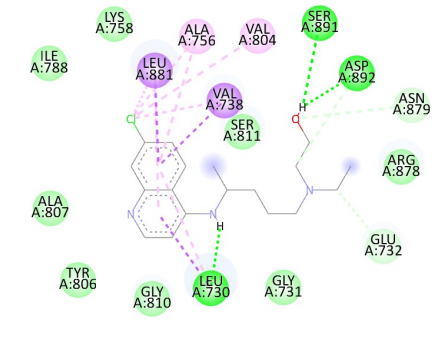
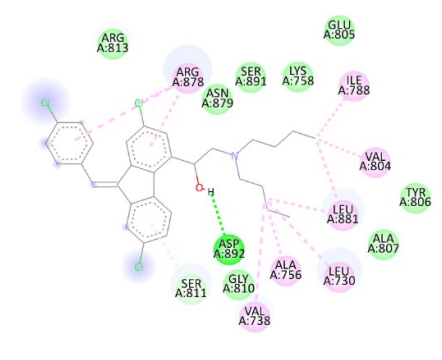
4	Chloroquine	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Ile1084 • Hydrophobic interactions: Tyr1230, Met1211, Ala1221, Ala1108, Leu1157, Val1092 • Miscellaneous interactions: Met1211 	<p>Interactions</p> <ul style="list-style-type: none"> Van der Waals Carbon Hydrogen Bond Pi-Sulfur Pi-Pi Stacked Alkyl Pi-Alkyl
5	Doxycycline	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Arg1086, Asn1167 • Hydrophobic interactions: Met1211, Val1092 	<p>Interactions</p> <ul style="list-style-type: none"> Van der Waals Conventional Hydrogen Bond Pi-Sigma Pi-Alkyl
6	Hydroxychloroquine	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Arg1086 • Hydrophobic interactions: Tyr1230, Met1211, Ala1221, Val1092, Ala1108, Leu1157 • Miscellaneous interactions: Met1211 	<p>Interactions</p> <ul style="list-style-type: none"> Van der Waals Conventional Hydrogen Bond Pi-Sulfur Pi-Pi Stacked Alkyl Pi-Alkyl

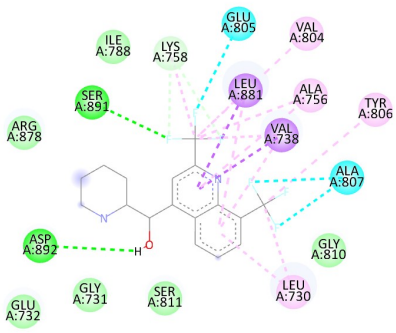
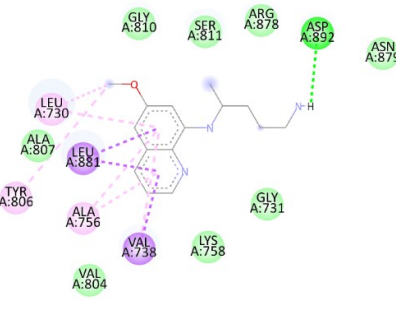
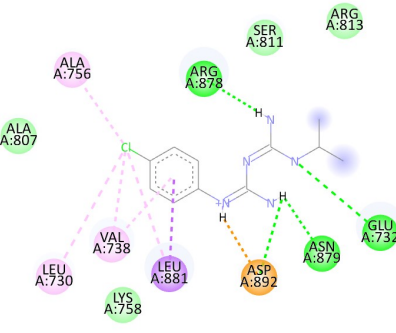
7	Lumefantrine	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Lys1161, met 1160 • Hydrophobic interactions: Tyr230, Met1211, Val1092, Ala1108, Leu1157, Lys1161 • Electrostatic interactions: Asp1164 • Miscellaneous interactions: Asp1164 • Unfavourable interactions: Ile1084 	<p>Interactions</p> <ul style="list-style-type: none"> van der Waals Conventional Hydrogen Bond Carbon-Hydrogen Bond Halogen (Fluorine) Pi-Sulfur Pi-Pi Stacked Alkyl Pi-Alkyl Pi-Sigma
8	Mefloquine	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Arg1086, Asp1164 • Hydrophobic interactions: Tyr230, Met1211, Ala1221, Met 1160, Leu1157, Leu1140, Ala1108, Val1092 • Halogen Interactions: Asn1209, Arg1208, Pro1158 • Miscellaneous interactions: Met1211 	<p>Interactions</p> <ul style="list-style-type: none"> van der Waals Conventional Hydrogen Bond Carbon-Hydrogen Bond Halogen (Fluorine) Pi-Sulfur Pi-Pi Stacked Alkyl Pi-Alkyl Pi-Sigma
9	Primaquine	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Ile1084 • Hydrophobic interactions: Tyr230, Ala1221 • Miscellaneous interactions: Met1211 	<p>Interactions</p> <ul style="list-style-type: none"> van der Waals Conventional Hydrogen Bond Pi-Sulfur Pi-Pi Stacked Pi-Alkyl

10	Proguanil	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Asp1164, Arg1208 • Hydrophobic interactions: Tyr1230, Ala1221, Ala1226, Leu1140 • Electrostatic interactions: Tyr1230, Asp1164 • Miscellaneous interactions: Met1211 	<p>Interactions</p> <ul style="list-style-type: none"> van der Waals Attractive Charge Conventional Hydrogen Bond Pi-Cation Pi-Sulfur Pi-Pi Stacked Alkyl Pi-Alkyl
11	Pyrimethamine	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Arg1208 • Hydrophobic interactions: Tyr1230, Met1211, Val1092 • Miscellaneous interactions: Met1211 	<p>Interactions</p> <ul style="list-style-type: none"> van der Waals Conventional Hydrogen Bond Pi-Cation Pi-Sulfur Pi-Pi Stacked Alkyl Pi-Alkyl
12	Quinine	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Tyr1230 • Hydrophobic interactions: Tyr1230, Met1211, Ala1221, Ala1226, Leu1157, Val1092, Ala1108 • Miscellaneous interactions: Met1211 	<p>Interactions</p> <ul style="list-style-type: none"> van der Waals Carbon Hydrogen Bond Pi-Donor Hydrogen Bond Pi-Sulfur Pi-Pi Stacked Alkyl Pi-Alkyl

13	Sulfadoxine	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Pro1158, Met1160, Arg1208, Asn1209, Tyr1230 • Hydrophobic interactions: Tyr1230, Met1211, Ala1221, Val1092, Ala1108 • Miscellaneous interactions: Met1211 	
14	Tafenoquine	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Gly1085, Tyr1230, Asn1167, Asp1164 • Hydrophobic interactions: Tyr1230, Met1211, Val1092, Leu1157 	
RET			
1	Artemether	<ul style="list-style-type: none"> • Hydrophobic interactions: Val738 	

2	Artesunate	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Ser811, Gly731 • Hydrophobic interactions: Leu730, Leu881 	 <p>Interactions</p> <ul style="list-style-type: none"> van der Waals Conventional Hydrogen Bond Carbon Hydrogen Bond Alkyl
3	Atovaquone	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Lys758 • Hydrophobic interactions: Leu730, Leu881, Val738, Ala756, Ala807, Arg878 	 <p>Interactions</p> <ul style="list-style-type: none"> van der Waals Conventional Hydrogen Bond Carbon Hydrogen Bond Pi-Sigma Pi-Alkyl
4	Chloroquine	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Ala807, Glu732 • Hydrophobic interactions: Leu730, Val738, Ala756, Ala807, Leu881 	 <p>Interactions</p> <ul style="list-style-type: none"> van der Waals Conventional Hydrogen Bond Carbon Hydrogen Bond Pi-Sigma Alkyl Pi-Alkyl

5	Doxycycline	<ul style="list-style-type: none"> Hydrogen bonding interactions: Arg813, Gly731, Glu732, Gly733, Ser811 	 <p>Interactions</p> <ul style="list-style-type: none"> van der Waals Conventional Hydrogen Bond Carbon Hydrogen Bond
6	Hydroxychloroquine	<ul style="list-style-type: none"> Hydrogen bonding interactions: Ser891, Asp892, Asn879, Glu732, Leu730 Hydrophobic interactions: Leu730, Leu881, Val738, Ala756, Val804 	 <p>Interactions</p> <ul style="list-style-type: none"> van der Waals Conventional Hydrogen Bond Carbon Hydrogen Bond Pi-Sigma Alkyl Pi-Alkyl
7	Lumefantrine	<ul style="list-style-type: none"> Hydrogen bonding interactions: Ser811, Asp892 Hydrophobic interactions: Leu730, Leu881, Val738, Ala756, Arg878, Ile788, Val804 	 <p>Interactions</p> <ul style="list-style-type: none"> van der Waals Conventional Hydrogen Bond Pi-Donor Hydrogen Bond Alkyl Pi-Alkyl

8	Mefloquine	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Asp892, Ser891, Lys758 • Hydrophobic interactions: Lys758, Leu881, Val738, Val804, Ala756, Tyr806, Leu730 • Halogen Interactions: Glu805, Ala807 	 <p>Interactions</p> <ul style="list-style-type: none"> van der Waals Conventional Hydrogen Bond Carbon Hydrogen Bond Halogen (Fluorine) Pi-Sigma Allyl Pi-Allyl
9	Primaquine	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Asp892 • Hydrophobic interactions: Leu881, Val738, Leu730, Tyr806, Ala756 	 <p>Interactions</p> <ul style="list-style-type: none"> van der Waals Conventional Hydrogen Bond Pi-Sigma Allyl Pi-Allyl
10	Proguanil	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Arg878, Glu732, Asn879, Asp892 • Hydrophobic interactions: Ala756, Leu881, Val738, Leu730 • Electrostatic interactions: Asp892 	 <p>Interactions</p> <ul style="list-style-type: none"> van der Waals Salt Bridge Conventional Hydrogen Bond Pi-Sigma Allyl Pi-Allyl

11	Pyrimethamine	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Asp892, Glu805, Lys758 • Hydrophobic interactions: Leu730, Ala756, Leu881, Val738 	<p>Interactions</p> <ul style="list-style-type: none"> van der Waals Conventional Hydrogen Bond Carbon Hydrogen Bond Pi-Sigma Pi-Alkyl
12	Quinine	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Ser891 • Hydrophobic interactions: Leu881, Leu730, Ala756, Val738, Ala807 	<p>Interactions</p> <ul style="list-style-type: none"> van der Waals Conventional Hydrogen Bond Carbon Hydrogen Bond Pi-Sigma Pi-Alkyl
13	Sulfadoxine	<ul style="list-style-type: none"> • Hydrogen bonding interactions: Glu805, Gly733, Asn879 • Hydrophobic interactions: Ala807, Leu881, Leu730, Ala756, Val738, Arg878 	<p>Interactions</p> <ul style="list-style-type: none"> van der Waals Conventional Hydrogen Bond Carbon Hydrogen Bond Pi-Sigma Pi-Alkyl

14

Tafenoquine

- **Hydrogen bonding interactions:**
Ser891, Lys758,
Ser811, Arg878
- **Hydrophobic interactions:**
Leu881, Val738,
Ala756, Ala807,
Leu730, Val804
- **Halogen Interactions:**
Glu805

