Cholesterol and its influence in lipid membranes

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Biosynthetic pathway for synthesis of cholesterol

Lanosterol, Cholesterol,

Lipid Compositions of Some Biological Membranes

<table>
<thead>
<tr>
<th>Lipid</th>
<th>Human Erythrocyte</th>
<th>Human Myelin</th>
<th>Beef Heart Mitochondria</th>
<th>E. coli</th>
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<tbody>
<tr>
<td>Phosphatidic acid</td>
<td>1.5</td>
<td>0.5</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Phosphatidylcholine</td>
<td>19</td>
<td>10</td>
<td>39</td>
<td>0</td>
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<td>Phosphatidylethanolamine</td>
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<td>20</td>
<td>27</td>
<td>65</td>
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<td>Phosphatidylglycerol</td>
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<td>0</td>
<td>18</td>
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<tr>
<td>Phosphatidylinositol</td>
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<td>1</td>
<td>7</td>
<td>6</td>
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<td>Phosphatidylserine</td>
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<td>Cardiolipin</td>
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<td>Sphingomyelins</td>
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<td>Glycolipids</td>
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<td>Cholesterol</td>
<td>25</td>
<td>26</td>
<td>3</td>
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</tr>
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</table>

*The values given are weight percent of total lipid.
Phospholipids have different acyl chains

Dimensions of the phospholipids molecules

Dimensions of the phospholipids molecules and cholesterol

Exploring lateral heterogeneity in synthetic membranes

(a) Above transition temperature

fluid or “liquid”

(b) Below transition temperature

solid or “gel”
Lipid membrane phases

- Crystalline
- Gel
- Solid-ordered
- Ripple
- Liquid disordered

Phase transition and phases in DPPC

Phase diagram of lipid bilayers of binary mixtures of PC lipids
How does cholesterol affect the physical properties of lipids bilayers?

Phase diagram of lipid bilayers with cholesterol

DPPC DLPC phase diagram

Phase diagram of lipid bilayers with cholesterol

Liquid-crystalline, liquid-disordered
$T_l < T_c$ or $T_l < T_o$

Solid gel
$T_c < T_l < T_o$

Liquid-ordered, rigid
$T_c < T_l < T_r$

$S = \text{Low}$
$D_1 = \text{Fast} (-1 \mu m^2 s^{-1})$

$S = \text{High}$
$D_1 = \text{Slow} (10^{-2} \mu m^2 s^{-1})$
Lanosterol is unable to stabilize a liquid-ordered phase

Ternary phase diagram for POPC-SM-Cholesterol

Ternary phase diagram
Physical membrane properties regulated by cholesterol

- Permeability (ions, glucose, epicholesterol no effect)
- Binding of solutes (EtOH)
- Lateral diffusion (Modest effect, only below $T_m$)
- Condensing effect (monolayers)

Susceptibility of cholesterol to cholesterol oxidase on red blood cells

Rate of transfer of dehydrocholesterol to $\beta$-methyl cyclodextrin

Cholesterol homeostasis and the escape tendency (activity) of plasma membrane cholesterol.

Prog. Lip. Res. 2008, 47, 319-332
Cholesterol-dependent Cytolysins

- Synthesized and secreted by Gram-positive bacteria
- Bind and oligomerize on cholesterol-containing membranes
- Forms large transmembrane pores

Perfringolysin O (PFO)

- Synthesized and secreted as a water-soluble monomer (53 kDa)
- Binds to cholesterol-containing membranes
- Comprised of four different structural domains

Cholesterol Dependence of Domain 4-membrane Interaction

\[
\text{F/F}_0 = \frac{\text{Fluorescence with cholesterol}}{\text{Fluorescence without cholesterol}}
\]

\(\lambda_{ex} = 295 \text{ nm}\)
\(\lambda_{em} = 348 \text{ nm}\)

Heuck et al. (2000)
Molec. Cell 6, 1233