Supplementary text S1:

Commentation of criteria selected for patient subclassification

1) DRYaq: Patients with a BST $\leq 10$ and no pathologic TBUT ($>10$ s) were classified as aqueous deficient patients, due to the fact that a reduced production/secretion of tear fluid will predominantly result in a lower BST value.$^{1,2}$ With the purpose to get a representative insight into the tear proteome of patients suffering from different stages of aqueous deficient dry-eye, we choose a BST threshold of $\leq 10$ mm/5 min, in accordance with previous studies of our group and others.$^{3,4,5}$

2) DRYlip: Patients with a TBUT $\leq 10$ s and a normal Schirmer value ($>10$ mm/5 min) were classified as lipid deficient dry eye. A dysfunctional, thinned lipid layer goes along with a pathological/decreased TBUT,$^{6}$ which is due to the lower tear film stability.$^{7}$ However, the TBUT is not necessarily correlated with a decreased Schirmer value.$^{8}$ Thus, in the present study patients with a Schirmer value $>10$ mm/5 min and a TBUT $\leq 10$ s were specifically classified as lipid deficient dry-eye (DRYlip) subjects, as they reveal a normal aqueous state but a pathological tear film stability. Further, the occurrence of a lipid layer deficiency was assured by inspecting meibomian glands.$^{9}$ Patients with a score $\geq 18$ were classified as pathologic, respectively lipid deficient. Foulks and Bron suggested a threshold of $>10$. Due to the higher specificity we set a threshold of $\geq 18$.

3) DRYaqlip: Patients with a Schirmer value $\leq 10$ mm and a TBUT $\leq 10$ were classified as patients who suffer from a combined pathogenesis, means they are aqueous deficient as well as lipid deficient. It is generally accepted that symptoms of advanced stages of aqueous deficiency and lipid deficiency are overlapping and influencing each other. As suggested by Versura et al. 2010, a thin lipid layer results in an unstable tear film and an aqueous tear-deficient state; respectively an aqueous tear
deficient state results in a thin lipid layer. Thus, we classified patients with a pathologic BST, TBUT and optionally a score \( \geq 18 \) as aqueous and lipid deficient.


