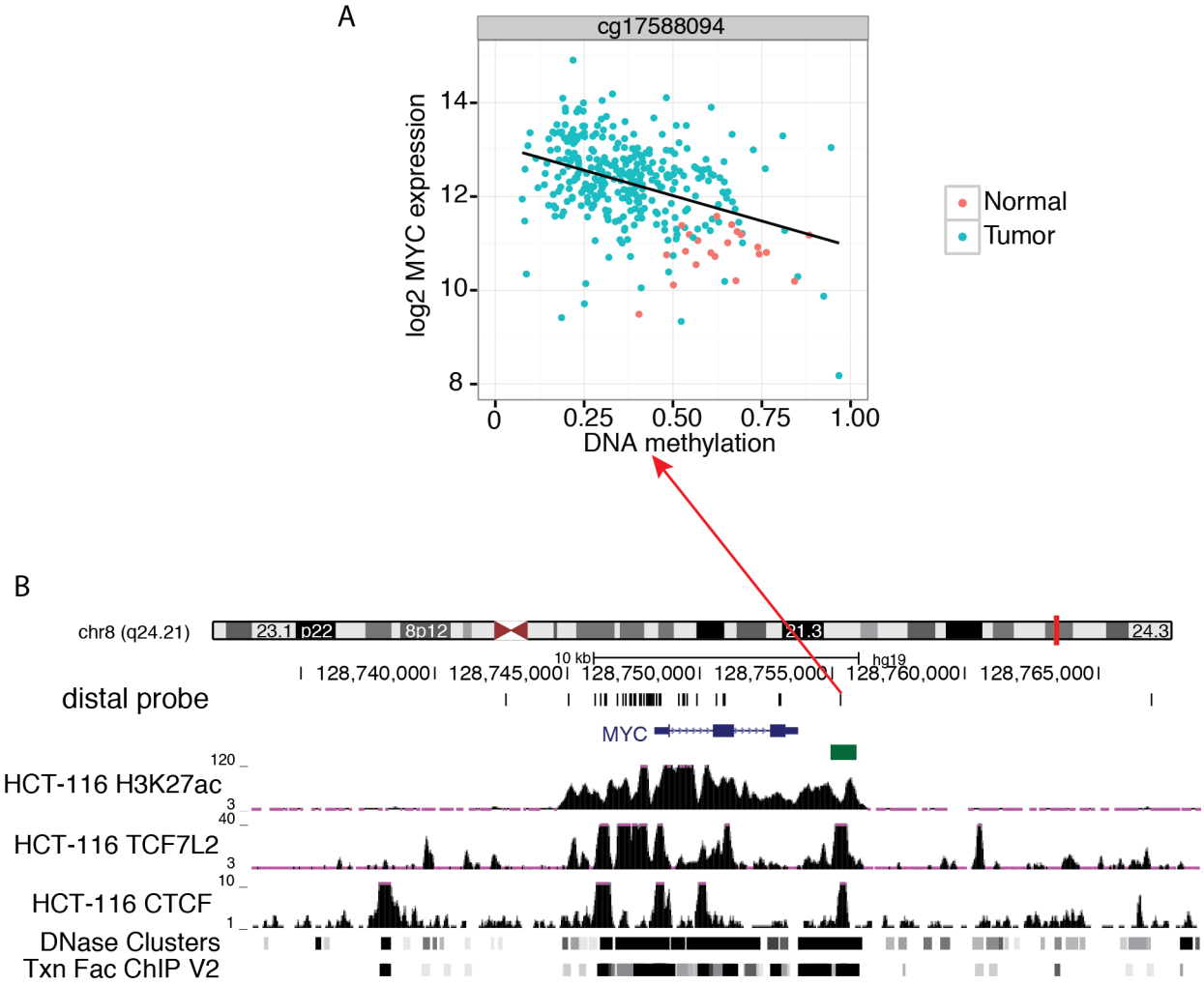Yao Additional file 14